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8-Amino*iso*quinoline: A correction. By K. SCHOFIELD

JOURNAL
OF
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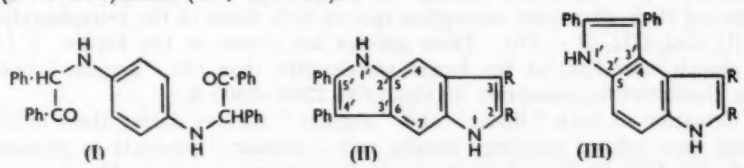
1. *The Synthesis and Structure of Some Pyrroloindoles.*

By D. A. KINSLEY and (the late) S. G. P. PLANT.

Benzoin has been condensed with *p*-phenylenediamine to give a mixture containing two tetraphenylpyrroloindoles, the structures of which have been determined by degradation of the " linear " 2 : 3 : 4′ : 5′-tetraphenylpyrrolo-(2′ : 3′-5 : 6)indole to *p*-dibenzoylbenzene. The structures of the products obtained by analogous condensations with 5-amino-2 : 3-dimethylindole are discussed. The preparation of other aminoindoles and their condensation products is described.

IN recent papers [1,2] it has been shown that the Japp–Murray synthesis [3] of indoles by which an aromatic amine is condensed with an α-hydroxy-ketone such as benzoin or 2-hydroxy*cyclo*hexanone [4] is a promising method for the preparation of pyrroloindoles and this communication describes the synthesis of some pyrroloindoles derived formally from *o*- and *p*-phenylenediamine. Similar compounds derived from *m*-phenylenediamine have been synthesised by Ruggli and his co-workers.[5]

Japp and Meldrum [6] prepared *NN*′-didesyl-*p*-phenylenediamine (I) from benzoin and *p*-phenylenediamine and stated that, when the compound was heated with zinc chloride, two substances, m. p. 318° and 335° respectively, were obtained but no further practical details were given. In the present investigation, the mixture obtained by repeating this reaction was separated into 2 : 3 : 4′ : 5′-tetraphenylpyrrolo(2′ : 3′-5 : 6)-indole (II; R = Ph) which was the major product and its isomer, 2 : 3 : 4′ : 5′-tetraphenyl-pyrrolo(3′ : 2′-4 : 5)indole (III; R = Ph).



(I) (II) (III)

The " linear " structure of the pyrroloindole (II; R = Ph) was established by degradation. Oxidation with chromic anhydride [7,8] in acetic acid gave 1 : 4-dibenzamido-2 : 5-dibenzoylbenzene (IV; R = Bz) from which 1 : 4-diamino-2 : 5-dibenzoylbenzene (IV; R = H) was obtained by hydrolysis with sulphuric acid. Tetrazotisation of this amine followed by treatment with hypophosphorous acid [9] provided *p*-dibenzoylbenzene

[1] Swindells and Tomlinson, *J.*, 1956, 1135.
[2] Carter, Katritzky, and Plant, *J.*, 1955, 337.
[3] Japp and Murray, *J.*, 1894, **65**, 889.
[4] Jones and Tomlinson, *J.*, 1953, 4114.
[5] Ruggli and Straub, *Helv. Chim. Acta*, 1938, **21**, 1084, and previous papers.
[6] Japp and Meldrum, *J.*, 1899, **75**, 1043.
[7] Gaudion, Hook, and Plant, *J.*, 1947, 1631.
[8] Schofield and Theobald, *J.*, 1949, 796.
[9] Cf. Kornblum in Adams, " Organic Reactions," John Wiley and Sons, New York, 1944, Vol. II, p. 262.

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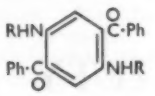
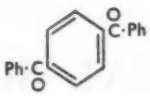
(V) identical (mixed m. p.) with a synthetic specimen. When the tetrazo-compound was heated at 100°, ring closure occurred giving 9 : 1′-dioxoindeno(3′ : 2′-2 : 3)fluorene (VI), the properties of which agreed with those given by Deuschel.[10]



(IV)



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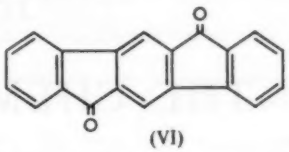
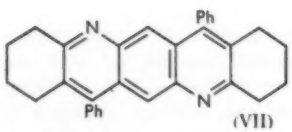


(VI)

The amine (IV; R = H) has also been condensed with *cyclo*hexanone, giving 6 : 7 : 8 : 9 : 5′ : 6′ : 7′ : 8′-octahydro-5 : 4′-diphenylquinolino(3′ : 2′-2 : 3)acridine (VII), aniline hydrochloride being used as a catalyst instead of alkali which is the usual catalyst in such reactions.[11]

It then seemed interesting to investigate the preparation of pyrroloindoles, analogous to those described above, by the interaction of benzoin with various aminoindoles. Accordingly, 5-amino-2 : 3-dimethylindole was heated with benzoin in the presence of a little hydrochloric acid. The mixture which was isolated was separated into 2 : 3-dimethyl-4′ : 5′-diphenyl-pyrrolo(2′ : 3′-5 : 6)indole (II; R = Me) and -pyrrolo(3′ : 2′-4 : 5)-indole (III; R = Me). Similarly, the product of the reaction between 5-amino-2 : 3-dimethylindole and 2-hydroxy*cyclo*hexanone in the presence of aniline hydrobromide[12] gave 5 : 6 : 7 : 8-tetrahydro-4′ : 5′-dimethylpyrrolo(3′ : 2′-2 : 3)carbazole (VIII) and its " angular " isomer (IX).



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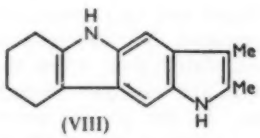

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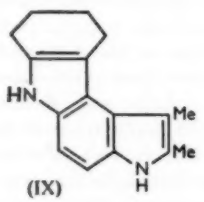

(IX)

These pyrroloindoles were markedly prone to oxidation and their solutions darkened in air, presumably owing to the formation of peroxides. Their structures were assigned by comparing their ultraviolet absorption spectra with those of the tetraphenylpyrroloindoles (II and III; R = Ph). These spectra are shown in the Figure. " Linear " isomers absorb more light at the longer wavelengths than the " angular " ones, and possess a characteristic absorption maximum at 2300—2500 Å.

The formation of both " linear " and " angular " isomers during these cyclisations is unusual since related reactions usually give " angular " products in preference to " linear " ones.[4,13] In the above " angular " products, however, there is probably considerable repulsion between the groups, phenyl or methyl, attached to the 3- and 4′-positions of the pyrroloindole (III; R = Ph or Me) or between the corresponding methyl and methylene groups in the pyrrolocarbazole (IX) and this will favour the formation of the linear products (II) and (VIII). An analogous situation occurs in 4 : 5-disubstituted phenanthrenes such as (X) in which hindrance between the methyl groups in the 4- and the 5-position causes asymmetry which has been demonstrated by resolution of the compound into optically active forms.[14] Bendas and Djerassi[15] have shown that the

[10] Deuschel, *Helv. Chim. Acta*, 1951, **34**, 2403.
[11] Cf. Albert, " The Acridines," Edward Arnold and Co., London, 1951, p. 62.
[12] Cf. Crowther, Mann, and Purdie, *J.*, 1943, 58.
[13] See, *e.g.*, Smith, *J. Amer. Chem. Soc.*, 1930, **52**, 397; Kulke and Manske, *Canad. J. Chem.*, 1952, **30**, 711.
[14] Newman and Hussey, *J. Amer. Chem. Soc.*, 1947, **69**, 3023.
[15] Bendas and Djerassi, *ibid.*, 1956, **78**, 2474.

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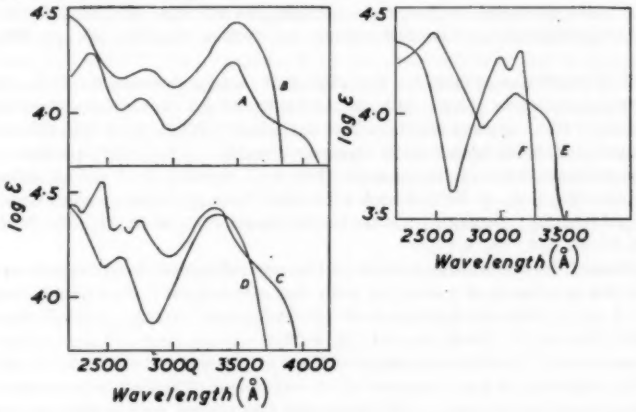
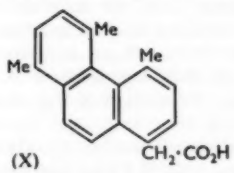
unexpected production of the anthracene nucleus in cyclisations which usually lead to the formation of phenanthrenes can be attributed to steric hindrance of this nature.

To extend these investigations to other aminoindoles, 4-, 5-, and 6-amino-2 : 3-diphenylindole were prepared by reduction of the corresponding nitro-compounds with dithionite, using the technique of Shaw and Woolley.[16] These amines were stable when

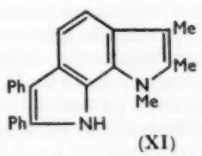
Absorption spectra of (*A*) 2 : 3 : 4′ : 5′-*tetraphenylpyrrolo*(2′ : 3′-5 : 6)*indole* (II; R = Ph), (*B*) 2 : 3 : 4′ : 5′-*tetraphenylpyrrolo*(3′ : 2′-4 : 5)*indole* (III; R = Ph), (*C*) 2 : 3-*dimethyl*-4′ : 5′-*diphenylpyrrolo*(2′ : 3′-5 : 6)*indole* (II; R = Me), (*D*) 2 : 3-*dimethyl*-4′ : 5′-*diphenylpyrrolo*(3′ : 2′-4 : 5)*indole* (III; R = Me), (*E*) 5 : 6 : 7 : 8-*tetrahydro*-4′ : 5′-*dimethylpyrrolo*(3′ : 2′-2 : 3)*carbazole* (VIII), *and* (*F*) 5 : 6 : 7 : 8-*tetrahydro*-4′ : 5′-*dimethylpyrrolo*(2′ : 3′-3 : 4)*carbazole* (IX) (*A*, *B*, *C*, *and D in* MeOH; *E and F in* EtOH).



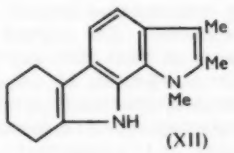
dry but, when wet with solvents, they underwent oxidation in air and became discoloured, the melting points being lowered. By reaction with ethyl acetoacetate, 5-amino-2 : 3-diphenylindole was converted into the corresponding indolylaminocrotonate, and with



(X)



(XI)



(XII)

benzaldehyde it yielded a Schiff's base which has been reduced catalytically to 5-benzylamino-2 : 3-diphenylindole. With benzoin a mixture was obtained from which the tetraphenylpyrroloindole (II; R = Ph) was isolated. When 6-amino-2 : 3-diphenylindole reacted with benzoin, 2 : 3 : 4′ : 5′-tetraphenylpyrrolo(2′ : 3′-4 : 5)indole, identical with the compound prepared by Japp and Meldrum [6] from *m*-phenylenediamine, was obtained. Although the reaction between benzoin and 4-amino-2 : 3-dimethylindole afforded 2 : 3-dimethyl-4′ : 5′-diphenylpyrrolo(2′ : 3′-4 : 5)indole, no product could be isolated from the analogous reaction with 6-amino-2 : 3-dimethylindole.

Although many nitroindoles can be conveniently reduced to amines with dithionite, this method was not satisfactory for the preparation of 7-amino-2 : 3-dimethylindole and 7-amino-1 : 2 : 3-trimethylindole, probably because these bases were particularly liable to oxidation during their isolation. Brown and Nelson [17] used Raney nickel and hydrazine

[16] Shaw and Woolley, *J. Amer. Chem. Soc.*, 1953, **75**, 1877.
[17] Brown and Nelson, *ibid.*, 1954, **76**, 5149.

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to prepare 6-aminoindole and in the present work this elegant technique gave the required 7-aminoindoles in yields of 50—75%.

When 7-amino-2 : 3-dimethylindole was heated with benzoin, and aniline hydrobromide as catalyst, no product could be isolated. Under the same conditions, however, 7-amino-1 : 2 : 3-trimethylindole gave the pyrroloindole (XI). In a similar way, 5 : 6 : 7 : 8-tetrahydro-1′ : 4′ : 5′-trimethylpyrrolo(2′ : 3′-1 : 2)carbazole (XII) was obtained when the amine was heated with 2-hydroxy*cyclo*hexanone.

Experimental

NN′-*Didesyl*-p-*phenylenediamine*.[6]—*p*-Phenylenediamine (12 g.) and benzoin (48 g.) were melted together at 140°, and hydrochloric acid (0·5 c.c.) was added. A vigorous reaction took place, and the mass solidified. The crude product (44 g.) was used directly in the following synthesis. It crystallised from *cyclo*hexanone as yellow rhombs, m. p. 250—257° (rapid heating).

2 : 3 : 4′ : 5′-*Tetraphenyl-pyrrolo*(2′ : 3′-5 : 6)*indole and -pyrrolo*(3′ : 2′-4 : 5)*indole*.—*NN′*-Didesyl-*p*-phenylenediamine (44 g.) and zinc chloride (27 g.) were ground together and heated at 200—210°, until the vigorous reaction had subsided. When cold, the solid was triturated with hot ethanol and then boiled with aqueous ethanol. The crude product (22 g.; m. p. 280—320°) crystallised from *cyclo*hexanone (300 c.c.), giving 2 : 3 : 4′ : 5′-*tetraphenylpyrrolo*-(2′ : 3′-5 : 6)*indole* (9 g.), m. p. 330°, which separated from pyridine as colourless needles, m. p. 331—333° (rapid heating), becoming yellow in air (Found: C, 88·5; H, 5·2; N, 5·8. $C_{34}H_{24}N_2$ requires C, 88·7; H, 5·2; N, 6·1%).

*cyclo*Hexanone, from the mother-liquors of the crystallisation described above, was removed in steam, and the residue was extracted with hot ethanol and crystallised three times from pyridine. 2 : 3 : 4′ : 5′-*Tetraphenylpyrrolo*(3′ : 2′-4 : 5)*indole* (1·4 g.) was obtained as needles, m. p. 310—312° (Found: C, 88·6; H, 5·4; N, 6·2%).

1 : 4-*Dibenzamido*-2 : 5-*dibenzoylbenzene*.—Finely powdered 2 : 3 : 4′ : 5′-tetraphenylpyrrolo(2′ : 3′-5 : 6)indole (5·8 g.), suspended in acetic acid (160 c.c.), was treated with chromic anhydride (3·6 g. in a little water), and the whole was stirred and heated on a water-bath for 2 hr. When cold, the solid residue of 1 : 4-*dibenzamido*-2 : 5-*dibenzoylbenzene* (1·7 g.), m. p. 293—296°, was washed with acetic acid and crystallised from pyridine, giving orange needles, m. p. 298° (Found: C, 77·6; H, 4·6; N, 5·3. $C_{34}H_{24}O_4N_2$ requires C, 77·9; H, 4·6; N, 5·3%).

1 : 4-*Diamino*-2 : 5-*dibenzoylbenzene*.—Sulphuric acid (48 c.c.) in water (32 c.c.) and 1 : 4-dibenzamido-2 : 5-dibenzoylbenzene (3·5 g.) were refluxed for 20 min. The hot solution was filtered (sintered-glass funnel), cooled, and after careful dilution with water was made alkaline with ammonia. The product (1·8 g.; m. p. 190—200°) separated from ethanol as crimson prisms, m. p. 204—206° with previous sintering, of 1 : 4-*diamino*-2 : 5-*dibenzoylbenzene* (1 g.) (Found: C, 75·9; H, 5·0. $C_{20}H_{16}O_2N_2$ requires C, 76·0; H, 5·1%). Treatment of this amine with benzoyl chloride in pyridine regenerated its benzoyl derivative.

Conversion of 1 : 4-*Diamino*-2 : 5-*dibenzoylbenzene into* p-*Dibenzoylbenzene*.—A stirred suspension of 1 : 4-diamino-2 : 5-dibenzoylbenzene (1 g.) in sulphuric acid (3·3 c.c.) and acetic acid (10 c.c.) was tetrazotised at 0—10° with sodium nitrite (0·5 g.). After hypophosphorous acid (6 g.) in water (16 c.c.) had been added, the whole was corked loosely and kept at 0° for 40 hr. The mass was extracted with benzene (300 c.c.)–ether (100 c.c.) and, after the extract had been washed successively with 2N-hydrochloric acid (2 × 50 c.c.), dilute ammonia (50 c.c.) and aqueous sodium carbonate (50 c.c.), it was dried ($MgSO_4$) and evaporated. The sticky residue was taken up in benzene and passed down a column of alumina (30 g.) and eluted with benzene. From the first eluate (175 c.c.), crude *p*-dibenzoylbenzene, m. p. 155—160°, was obtained by evaporation. The second fraction (475 c.c.) gave a mixture containing 9 : 1′-dioxoindeno(3′ : 2′-2 : 3)fluorene, which was purified by washing with a little benzene, a further quantity of *p*-dibenzoylbenzene, m. p. 147—157°, being recovered from the washings. The combined yield of *p*-dibenzoylbenzene (0·2 g.) crystallised from acetic acid in needles, m. p. 158—160°, not depressed by admixture with an authentic specimen prepared from terephthalic acid.[18]

9 : 1′-*Dioxoindeno*(3′ : 2′-2 : 3)*fluorene*.—The mixture obtained by tetrazotisation of 1 : 4-diamino-2 : 5-dibenzoylbenzene (0·8 g.) as described above was heated on a water-bath for ½ hr.,

[18] Munchmeyer, *Ber.*, 1886, **19**, 1845.

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until effervescence had ceased. After 12 hr. the precipitate was triturated with hot ammonia and taken up in benzene (500 c.c.). The solution was passed through alumina (15 g.) and was eluted with benzene. Evaporation of the first fraction gave a residue (0·06 g., m. p. 315—330°) which separated from acetic acid in violet needles of 9 : 1′-dioxoindeno(3′ : 2′-2 : 3)fluorene, m. p. 338—340° (Found: C, 84·8; H, 3·9. Calc. for $C_{16}H_{10}O_2$: C, 85·1; H, 3·5%). Deuschel [19] gives m. p. 345—346°.

6 : 7 : 8 : 9 : 5′ : 6′ : 7′ : 8′-*Octahydro*-5 : 4′-*diphenylquinolino*(3′ : 2′-2 : 3)*acridine*.—When 1 : 4-diamino-2 : 5-dibenzoylbenzene (1 g.), *cyclo*hexanone (0·8 g.), and a catalytic amount of aniline hydrochloride were heated together at 135°, steam was evolved and the mass solidified. After the solid had been washed with hot ethanol, the *quinolinoacridine* (0·5 g.), m. p. 380—390°, was obtained by crystallisation from anisole. Further crystallisation from anisole gave yellow prisms, m. p. 382—390° (black liquid), which for analysis were dried at 200° *in vacuo* (Found: C, 87·9, 87·9; H, 6·2, 6·4; N, 6·0, 6·0. $C_{32}H_{18}N_2$ requires C, 87·3; H, 6·4; N, 6·4%).

2 : 3-*Dimethyl*-4′ : 5′-*diphenyl-pyrrolo*(2′ : 3′-5 : 6)*indole and -pyrrolo*(3′ : 2′-4 : 5)*indole*. 5-Amino-2 : 3-dimethylindole [16] (7 g.), benzoin (9 g.), and hydrochloric acid (4 drops) were heated together at 205° until the melt solidified. After trituration with ethanol the crude mixture (9 g.), m. p. 235—245°, was crystallised three times from anisole, giving 2 : 3-*dimethyl*-4′ : 5′-*diphenyl-pyrrolo*(2′ : 3′-5 : 6)*indole* (0·9 g.) as plates, m. p. 285—287° (Found: C, 85·6; H, 6·1. $C_{24}H_{20}N_2$ requires C, 85·7; H, 6·0; N, 8·3%). After the anisole mother-liquors from the first of the above crystallisations had been boiled down almost to dryness, the material which separated was crystallised three times from anisole, and 2 : 3-*dimethyl*-4′ : 5′-*diphenylpyrrolo*(3′ : 2′-4 : 5)-*indole* (0·5 g.) was obtained as needles, m. p. 269—271° (rapid heating) (Found: C, 85·6; H, 6·2; N, 8·1%).

5 : 6 : 7 : 8-*Tetrahydro*-4′ : 5′-*dimethyl-pyrrolo*(3′ : 2′-2 : 3)*carbazole and -pyrrolo*(2′ : 3′-3 : 4)-*carbazole*.—After 5-amino-2 : 3-dimethylindole (3·4 g.) and 2-hydroxy*cyclo*hexanone (2·4 g.) had been heated together at 140° until evolution of water had subsided, aniline hydrobromide (0·05 g.) was added, and the melt heated to 200° until it solidified. The solid was ground with ethanol, and the crude mixture (1·9 g.), m. p. 240—280°, was crystallised from anisole giving 5 : 6 : 7 : 8-*tetrahydro*-4′ : 5′-*dimethylpyrrolo*(3′ : 2′-2 : 3)*carbazole* (0·8 g.) as prisms, m. p. 356—360° (rapid heating) (Found: C, 80·7; H, 7·8; N, 11·6. $C_{16}H_{18}N_2$ requires C, 80·7; H, 7·6; N, 11·8%). The anisole mother-liquors were rapidly evaporated to small bulk, and light petroleum (b. p. 40—60°) was added. The precipitated solid (1·1 g.), m. p. 225—255°, was crystallised twice from anisole. To minimise decomposition each crystallisation was carried out rapidly and the crystals were washed well with ethanol before being dried for a short time at 100°. 5 : 6 : 7 : 8-*Tetrahydro*-4′ : 5′-*dimethylpyrrolo*(2′ : 3′-3 : 4)*carbazole* (0·3 g.) separated as needles, m. p. 261—265°. Sublimation at 200°/2 × 10^{-4} mm. for 3½ hr. gave microcrystalline material, m. p. 263—267° (rapid heating) (Found: C, 80·4; H, 7·9%).

Nitro-2 : 3-*diphenylindoles*.—5-Nitro-2 : 3-diphenylindole,[19, 20] prepared from deoxybenzoin *p*-nitrophenylhydrazone, was obtained after purification (alumina) as prisms,[20] m. p. 200° (from ethanol), or needles,[19] m. p. 210° (from acetic acid). 4- and 6-Nitro-2 : 3-diphenylindole were prepared by separating the mixture obtained by the cyclisation of deoxybenzoin *m*-nitrophenylhydrazone.[19, 20]

6-Nitro-2 : 3-diphenylindole was more conveniently obtained by nitration.[21] Nitric acid (4 c.c.; *d* 1·5) in acetic acid (16 c.c.) was cautiously added to a hot solution of 2 : 3-diphenylindole (27 g.) in acetic acid (60 c.c.). The whole was boiled for 5 min. and the product (8 g.; m. p. 220—225°) which separated was collected. It crystallised from acetic acid in orange needles, m. p. 225—227°.

4- *and* 6-*Amino*-2 : 3-*diphenylindole*.—These were obtained in 70% yield by reduction of the corresponding nitroindoles with alkaline dithionite.[16] 4-*Amino*-2 : 3-*diphenylindole* crystallised from ethanol in plates, m. p. 202° (Found: C, 84·1; H, 5·6; N, 10·0. $C_{20}H_{16}N_2$ requires C, 84·5; H, 5·6; N, 9·9%). Its *acetyl derivative*, m. p. 197°, was obtained as rhombs (from ethanol) on treatment of the amine with acetic anhydride (Found: C, 80·9; H, 5·5. $C_{22}H_{18}ON_2$ requires C, 81·0; H, 5·5; N, 8·6%). 6-*Amino*-2 : 3-*diphenylindole* formed needles (from aqueous ethanol), m. p. 177° (Found: C, 84·3; H, 5·6; N, 9·7%), and its *acetyl derivative* crystallised from aqueous acetic acid in needles, m. p. 269° (Found: C, 80·9; H, 5·6%).

[19] Fennell and Plant, *J.*, 1932, 2872.
[20] Schofield and Theobald, *J.*, 1950, 1505.
[21] Bannister, B.A. Thesis, Oxford, 1947.

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5-Amino-2 : 3-diphenylindole.—A hot solution of 5-nitro-2 : 3-diphenylindole (11 g.) in ethanol (750 c.c.) and N-sodium hydroxide (150 c.c.) was treated with sodium dithionite (55 g.) in 0·5N-sodium hydroxide (220 c.c.). The light red solution was poured into water, and the crude product (8·5 g., m. p. 193—196°) was collected. For purification, it was distilled under reduced pressure and then crystallised from ethanol, giving *5-amino-2 : 3-diphenylindole* as plates, m. p. 202° (Found: C, 84·6; H, 5·7; N, 9·8%). The *hydrochloride* separated from ethanol in needles, m. p. 330° (Found: N, 9·1; Cl, 11·3. $C_{20}H_{17}N_2Cl$ requires N, 8·7; Cl, 11·1%). The *acetyl derivative* separated from aqueous ethanol in plates, m. p. 236° (Found: C, 81·1; H, 5·8; N, 8·5%).

5-Amino-2 : 3-diphenylindole (0·5 g.), ethyl acetoacetate (0·3 g.), and concentrated hydrochloric acid (1 drop) were ground together. After 12 hr., the solid (0·5 g.; m. p. 141°) obtained by trituration with ethanol crystallised from benzene–light petroleum, giving *ethyl* β-(*2 : 3-diphenylindol-5-yl*)*aminocrotonate* as needles, m. p. 142° (Found: C, 78·7; H, 6·0; N, 7·2. $C_{24}H_{24}O_2N_2$ requires C, 78·8; H, 6·1; N, 7·1%).

5-Benzylidene- and 5-Benzyl-amino-2 : 3-diphenylindole.—After 5-amino-2 : 3-diphenylindole (0·95 g.) and benzaldehyde (0·35 g.) had been heated to 120° for 10 min., crystallisation of the solid from methanol gave yellow needles (0·9 g.; m. p. 85—95°) containing solvent of crystallisation which was removed by drying first at 60° and then at 135° *in vacuo* for 10 hr., *5-benzylideneamino-2 : 3-diphenylindole* being obtained as brown rhombs, m. p. 158° (previous sintering) (Found: C, 86·9; H, 5·5. $C_{27}H_{20}N_2$ requires C, 87·1; H, 5·4%).

This compound (0·9 g., containing methanol of crystallisation) in methanol (150 c.c.) was shaken with hydrogen in the presence of 1% palladium–strontium carbonate (0·4 g.) until absorption ceased (5 hr., 88 c.c.; H_2 requires 54 c.c.). After the solution had been boiled, filtered whilst hot, and evaporated, the residue separated from ethanol in plates, m. p. 153°, of *5-benzylamino-2 : 3-diphenylindole* (0·2 g.) (Found: C, 86·3; H, 6·0. $C_{27}H_{22}N_2$ requires C, 86·6; H, 5·9%).

Treatment of this amine with acetic anhydride in benzene gave the *acetyl derivative*, which separated from ethanol in needles. These were dried at 210° *in vacuo* leaving the solvent-free derivative, m. p. 233° (Found: C, 83·3; H, 5·9. $C_{29}H_{24}ON_2$ requires C, 83·7; H, 5·8%).

Condensations with Benzoin.—(*a*) After 6-amino-2 : 3-diphenylindole (0·6 g.), benzoin (0·4 g.), and hydrochloric acid (1 drop) had been heated at 210° until the melt solidified, the solid was washed with ethanol, and the crude product (0·65 g., m. p. 271—279°) was crystallised three times from anisole, giving 2 : 3 : 4′ : 5′-tetraphenylpyrrolo(2′ : 3′-4 : 5)indole in needles, m. p. 282°, identical (mixed m. p.) with an authentic sample prepared from *m*-phenylenediamine.[4, 6]

(*b*) 5-Amino-2 : 3-diphenylindole (0·6 g.) and benzoin (0·4 g.) were condensed in the same way and the product (0·5 g.), m. p. 280—315°, was crystallised first from *cyclo*hexanone and then twice from pyridine, giving yellow needles of 2 : 3 : 4′ : 5′-tetraphenylpyrrolo(2′ : 3′-5 : 6)-indole, m. p. 333°, not depressed by admixture with a specimen prepared (see above) from *NN′*-didesyl-*p*-phenylenediamine.

(*c*) 4-Amino-2 : 3-dimethylindole [5, 11] (0·4 g.), benzoin (0·5 g.), and a catalytic quantity of aniline hydrobromide [12] were condensed together at 215°. The product (0·35 g.; m. p. 247—251°) obtained by trituration with ethanol was crystallised from anisole, to give 2 : 3-*dimethyl-4′ : 5′-diphenylpyrrolo*(2′ : 3′-4 : 5)*indole*, m. p. 250°, which for analysis was sublimed at 180°/3 × 10^{-4} mm. (Found: N, 8·2. $C_{24}H_{20}N_2$ requires N, 8·3%).

7-Amino-2 : 3-dimethylindole.—2 : 3-Dimethyl-7-nitroindole (1 g.) in warm methanol (60 c.c.) was treated alternately with small portions of Raney nickel and aqueous hydrazine (60%), so that gas was continuously evolved from the mixture, which was boiled occasionally. After ½ hr., when the yellow colour had been discharged, the solution was boiled to remove any excess of hydrazine, and was filtered. The filtrate was evaporated and the residue dried in a desiccator over potassium hydroxide. The *amine* then separated from carbon tetrachloride in needles (0·55 g.), m. p. 125—129°. Sublimation at 120°/4 × 10^{-3} mm. provided needles, m. p. 127—129° [Blackhall and Thomson [22] give m. p. 126° (decomp)] (Found: C, 74·7; H, 7·4. Calc. for $C_{10}H_{12}N_2$: C, 75·0; H, 7·5%). Treatment of the amine with acetic anhydride afforded the *acetyl derivative* as needles, m. p. 167° (from ethanol) (Found: C, 71·5; H, 7·1. $C_{12}H_{14}ON_2$ requires C, 71·3; H, 6·9%).

1 : 2 : 3-*Trimethyl-7-nitroindole.*—After 2 : 3-dimethyl-7-nitroindole [5] (17·5 g.), potassium hydroxide (44 g.) in water (14 c.c.), dimethyl sulphate (40 c.c.), and acetone (300 c.c.) had been

[22] Blackhall and Thomson, *J.*, 1954, 3916.

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refluxed together for ½ hr., addition of water precipitated 1 : 2 : 3-*trimethyl*-7-*nitroindole* (18·5 g.; m. p. 89—93°) which separated from ethanol in yellow prisms, m. p. 93° (Found: C, 64·7; H, 5·8. $C_{11}H_{12}O_2N_2$ requires C, 64·7; H, 5·9%).

7-*Amino*-1 : 2 : 3-*trimethylindole*.—1 : 2 : 3-Trimethyl-7-nitroindole (3 g.) in methanol (40 c.c.) was reduced with Raney nickel and hydrazine, by the technique described above. The residue obtained by evaporation of the methanol was dried over potassium hydroxide and triturated with a little ether, giving the crude product (1·2 g.; m. p. 139—143°). Sublimation at 110°/4 × 10^{-2} mm. gave the *amine* as needles, m. p. 146° (previous sintering) (Found: C, 75·9; H, 8·2. $C_{11}H_{14}N_2$ requires C, 75·9; H, 8·1%). Its *acetyl derivative* crystallised from methanol in needles, m. p. 189° (Found: C, 71·9; H, 7·2. $C_{13}H_{14}ON_2$ requires C, 72·2; H, 7·4%)

1 : 2 : 3-*Trimethyl*-4′ : 5′-*diphenylpyrrolo*(3′ : 2′-6 : 7)*indole*.—After 7-amino-1 : 2 : 3-trimethylindole (0·35 g.) and benzoin (0·4 g.) had been condensed together at 200° with aniline hydrobromide as catalyst, the solid was washed with ethanol, and the product (0·55 g.; m. p. 243—250°) was crystallised twice from anisole, giving the *pyrroloindole* as prisms, m. p. 256° (previous sintering) (Found: C, 85·4; H, 6·5. $C_{25}H_{22}N_2$ requires C, 85·7; H, 6·3%).

5 : 6 : 7 : 8-*Tetrahydro*-1′ : 4′ : 5′-*trimethylpyrrolo*(2′ : 3′-1 : 2)*carbazole*.—7-Amino-1 : 2 : 3-trimethylindole (1·2 g.) was heated with 2-hydroxy*cyclo*hexanone (0·8 g.) and aniline hydrobromide. At 165°, the melt solidified and the product (1·4 g.) was crystallised from anisole, and was then sublimed at 180°/8 × 10^{-2} mm., giving the *carbazole* as needles, m. p. 242—244° (Found: C, 80·8; H, 7·8. $C_{17}H_{20}N_2$ requires C, 81·0; H, 7·9%).

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2. *Azonitriles as Initiators for Polymerization of Methyl Methacrylate.*

By (the late) N. G. SAHA, U. S. NANDI, and SANTI R. PALIT.

The polymerization of methyl methacrylate, both homogeneous and in toluene and ethyl acetate, has been initiated with six azonitriles at 60°. The kinetic order with respect to initiator concentration is 0·5, and to monomer concentration 1·1 and 1·0 in toluene and ethyl acetate respectively. A mean value of 8·32 is obtained for δ (60°) from bulk-polymerization experiments with all six azonitriles.

The rates of initiation of all the azonitriles are about the same except that of azo*cyclo*hexane-1 : 1′-dicarbonitrile which is slightly lower. Efficiencies are all about 82% in bulk and decrease on dilution to about 50%.

The chain-transfer coefficients for monomer (C_M), initiator (C_I), and solvents (C_S) were determined. C_M is 1·0 × 10^{-5} whereas C_I is very close to zero in all cases. The chain-transfer coefficients for two solvents were also determined by using four of these catalysts and the results agree well with the literature values.

AZONITRILES decompose more cleanly, without complicating side effects,[1] than benzoyl peroxides previously used [2] to polymerize methyl methacrylate. We now report polymerizations initiated with six azonitriles at 60°.

Dependence of the Rate of Polymerization, R_p, on Catalyst Concentration.—Table 1 and

[1] Nozaki and Bartlett, *J. Amer. Chem. Soc.*, 1946, **68**, 1686; Bartlett and Nozaki, *ibid.*, 1947, **69**, 2299; Cass, *ibid.*, 1946, **68**, 1976.

[2] (*a*) Saha, Nandi, and Palit; *J.*, 1956, **85**, 427; (*b*) Palit, *Proc. Nat. Acad. Sci.*, 1954, **23**, *A*, 11.

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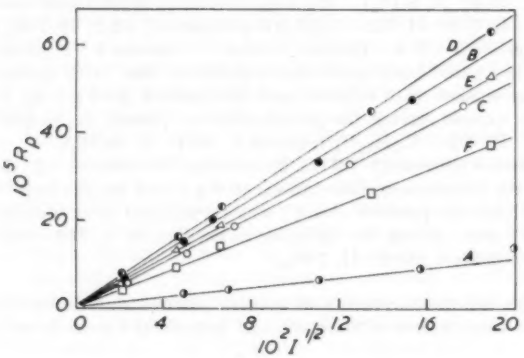
the Figure show that in all cases R_p is proportional to $I^{\frac{1}{2}}$ in agreement with the usual equation

$$R_p = KI^{\frac{1}{2}} M^n \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where I and M are the initiator and monomer concentrations respectively, and K is a constant. The straight lines pass through the origin, showing that there is practically no inhibition period and very little superimposed thermal reaction, and termination is



Dependence of rate of polymerization R_p on the initiator concentration. For catalysts, see Table 1.

TABLE 1. *Polymerization of methyl methacrylate in bulk* (9·29 *moles* $l.^{-1}$) *in presence of catalysts at* 60°.

$10^3(I/M)$	$10^5 R_p$ (moles $l.^{-1}$ $sec.^{-1}$)	$10^5/\overline{P}$	
Azo*cyclo*hexane-1 : 1′-dicarbonitrile (*A*)			
4·30	13·5	11·86	$10^4 R_p/I^{\frac{1}{2}} = 7·0$
2·65	9·0	8·17	$\delta = 8·32$
1·33	6·6	5·69	$10^7 R_t/I = 7·86$
0·53	4·2	4·33	$C_I = \sim 0$
0·27	3·2	3·65	$10^4 C_M = 1·0$
αα′-Azo*iso*butyronitrile (*B*)			
2·62	47·3	38·62	$10^3 R_p/I^{\frac{1}{2}} = 3·0$
1·31	33·2	27·98	$\delta = 8·32$
0·52	20·4	17·00	$10^6 R_t/I = 14·44$
0·26	14·8	12·96	$C_I = \sim 0$
0·05	6·5	6·13	$10^5 C_M = 1·0$
αα′-Azo-α-methylbutyronitrile (*C*)			
3·35	46·0	37·56	$10^3 R_p/I^{\frac{1}{2}} = 2·5$
1·68	32·9	27·37	$\delta = 8·32$
0·56	18·9	16·50	$10^6 R_t/I = 10·02$
0·28	12·5	9·50	$C_I = \sim 0$
0·06	6·1	5·46	$10^5 C_M = 1·0$

$10^3(I/M)$	$10^5 R_p$ (moles $l.^{-1}$ $sec.^{-1}$)	$10^5/\overline{P}$	
αα′-Azo-α-methylvaleronitrile (*D*)			
3·90	62·5	52·02	$10^3 R_p/I^{\frac{1}{2}} = 3·33$
1·95	44·5	38·08	$\delta = 8·32$
0·48	23·0	21·04	$10^6 R_t/I = 17·79$
0·24	16·2	15·15	$C_I = \sim 0$
0·05	7·5	6·00	$10^5 C_M = 1·0$
αα′-Azo-αββ-trimethylbutyronitrile (*E*)			
3·90	52·5	44·10	$10^3 R_p/I^{\frac{1}{2}} = 2·8$
0·48	19·0	17·00	$\delta = 8·32$
0·24	13·3	12·57	$10^6 R_t/I = 12·57$
0·05	6·0	4·89	$C_I = \sim 0$
			$10^5 C_M = 1·0$
αα′-Azo-α-ethylbutyronitrile (*F*)			
3·90	37·1	31·39	$10^3 R_p/I^{\frac{1}{2}} = 2·0$
1·95	26·2	22·82	$\delta = 8·32$
0·48	13·8	11·99	$10^6 R_t/I = 6·42$
0·24	9·2	7·48	$C_I = \sim 0$
0·05	4·6	4·26	$10^5 C_M = 1·0$

probably by a bimolecular free-radical interaction. This behaviour was observed by Overberger, Fram, and Alfrey [3] in the polymerization of styrene by αα′-azo*iso*butyronitrile and azo*cyclo*hexane-1 : 1′-dicarbonitrile and by Arnett [4] in αα′-azo*iso*butyronitrile-initiated polymerization of methyl methacrylate. However, Thomas and Pellon [5a] found R_p to be proportional to $I^{0·75}$ in the benzoyl peroxide-initiated bulk polymerization of

[3] Overberger, Fram, and Alfrey, *J. Polymer Sci.*, 1951, **6**, 539.
[4] Arnett, *J. Amer. Chem. Soc.*, 1952, **74**, 2027.
[5] (*a*) Thomas and Pellon, *J. Polymer Sci.*, 1954, **13**, 329; (*b*) Andreconix and Smets, *ibid.*, 1953, **10**, 525; (*c*) Horikx and Hermans, *ibid.*, 1953, **11**, 325.

acrylonitrile. This unusual behaviour might be due to the separation of phase in acrylonitrile polymerization. With substituted benzoyl peroxides [2] and hydrogen peroxide [6f] we found R_p to be proportional to $I^{0.5}$.

Dependence of R_p on Monomer Concentration.—Since the expected kinetic order of 3/2 with respect to monomer concentration is often not obtained [3, 4, 5a, 5b, 6f] we determined the kinetic order with respect to monomer with different azonitriles in solutions of ethyl acetate and toluene. Eqn. (1) can be reduced to the form

$$R_p = K(I/M)^{\frac{1}{2}} M^{(n+\frac{1}{2})} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where n is the order of the reaction with respect to the monomer. By plotting log R_p against log M at constant I/M, n was found (Table 2). In toluene n is 1·1 and 1·0 with

TABLE 2. *Dependence of R_p on monomer concentration at* 60°.

Catalyst	Solvent					
B	Toluene	$10^4 I/M$	13·12	6·56	3·28	0·66
		n	1·1	1·2	1·1	1·1
A	Toluene	$10^4 I/M$	44·00	22·00	11·00	
		n	1·0	1·0	1·05	
B	Ethyl acetate	$10^4 I/M$	13·12	6·56	3·28	0·66
		n	1·1	1·1	1·1	1·1

αα-azo*iso*butyronitrile and azo*cyclo*hexane-1 : 1′-dicarbonitrile respectively. In ethyl acetate with αα-azo*iso*butyronitrile the order is 1·0. Arnett [4] found n to be unity in benzene in the polymerization of methyl methacrylate by αα′-azo*iso*butyronitrile whereas Overberger, Fram, and Alfrey [3] report 1·2 for styrene in toluene with αα′-azo*iso*butyronitrile and azo*cyclo*hexane-1 : 1′-dicarbonitrile as catalysts.

Value of $\delta(= k_t^{\frac{1}{2}}/k_p)$.—For methyl methacrylate many different values of δ have been obtained.[2, 6] The general equation [2b, 6d] for the average degree of polymerization is

$$1/\overline{P} = \sum C_X \cdot X/M = C_M + C_I(I/M) + C_S(S/M) + R_p(\delta^2/M^2) \quad . \quad . \quad (3)$$

With all azonitriles (see later) C_I is consistently near zero. For bulk conditions, eqn. (3) becomes

$$1/\overline{P} = C_M + (\delta^2/M^2)R_p \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

Hence a plot of $1/\overline{P}$ against R_p should be a straight line from whose slope δ can be evaluated. For the six azonitriles we found a mean value of 8·32 (Table 1) for δ for methyl methacrylate at 60° [cf. 8·43 (Nandi and Palit [6f]), 8·3 (obtained from the absolute values of k_p and k_t (Matheson *et al.*[6c]), and 8·3 (Baysal and Tobolsky [6d])]. We conclude that the correct value of δ lies between 8·3 and 8·4.

Rates of Initiation.—At the steady state during polymerization [6d, 7]

$$R_i = 2\,k_t(M^*)^2 = 2(k_i/k_p^2)(R_p^2/M^2) \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

$$R_i/I = 2(k_i/k_p^2)(R_p^2/I)(1/M^2) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

$$= (2\,\delta^2/M^2)(R_p^2/I) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

Since R_p^2/I is constant, R_i/I should be constant for a particular monomer concentration. R_p^2/I has been taken from Table 1 and values of R_i/I are listed in Table 3, which shows that the specific initiation rates for all the azonitriles are of the same order of magnitude. Thus

[6] (*a*) Bonsal, Valentine, and Melville, *Trans. Faraday Soc.*, 1952, **48**, 765; (*b*) Bamford and Dewar, *Discuss. Faraday Soc.*, 1947, **2**, 310; (*c*) Matheson, Auer, Bevilacqua, and Hart, *J. Amer. Chem. Soc.*, 1949, **71**, 497; (*d*) Baysal and Tobolsky, *J. Polymer Sci.*, 1952, **8**, 529; (*e*) Melville and Burnett, *ibid.*, 1954, **13**, 417; (*f*) Nandi and Palit, *ibid.*, 1955, **17**, 65.

[7] Tobolsky and Baysal, *J. Polymer Sci.*, 1953, **11**, 471.

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the reactivities of the radicals formed are all about the same. The slightly lower rate of initiation observed with azo*cyclo*hexane-1 : 1′-dicarbonitrile may be due to the cyclic structure of the radical reducing the number of effective collisions bringing about initiation.

TABLE 3. *Rates of initiation and efficiency of catalysts in solutions at* 60°.

Solvent	Catalyst	Monomer concn. (moles l.$^{-1}$)	$10^6R_i/I$	f	Solvent	Catalyst	Monomer concn. (moles l.$^{-1}$)	$10^6R_i/I$	f
Nil	*B*	9·290	14·4	0·83	Ethyl acetate	*B*	4·645	10·5	0·60
							2·790	8·5	0·49
Nil	*C*	9·290	10·0	0·82			1·858	6·6	0·38
							0·929	6·8	0·39
Nil	*D*	9·290	17·8	0·87					
					Toluene	*A*	4·645	0·4	—
Toluene	*B*	4·675	11·5	0·60			2·790	0·4	—
		2·790	8·5	0·49			1·858	0·4	—
		1·858	6·8	0·39			0·929	0·4	—
		0·929	5·3	0·30					
					Toluene	*C*	4·645	6·9	0·56
							2·790	6·0	0·50
							1·858	6·4	0·53
							0·929	5·8	0·48

The value of $1{\cdot}44 \times 10^{-5}$ for R_i/I in αα′-azo*iso*butyronitrile agrees with the value of $1{\cdot}48 \times 10^{-5}$ obtained by Baysal and Tobolsky [6d] for the same catalyst and conditions.

Catalyst Efficiency (f).—The azonitriles undergo a first-order decomposition, presumably into a radical pair, at very nearly the same rate [4, 8, 9, 10] in all solvents:

$$-\mathrm{d}I/\mathrm{d}t = k_dI \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

where k_d is the specific rate constant for spontaneous homolytic cleavage. Hence the rate at which uniradical catalyst fragments are being produced by the catalyst is $2k_dI$ and the catalyst efficiency is properly defined as

$$f = R_i/(2\ k_dI) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

The factor f represents the fraction of the free radicals, produced by the decomposition of azonitriles, initiating polymerization. The values of k_d at 60° for different catalysts were calculated from those reported by Overberger, Shaugnessy, and Shalit [8] at 80·2 and 69·8°. The values of R_i/I at 60° just obtained were used to determine f (Table 3).

The value of 0·83 for f for αα′-azo*iso*butyronitrile agrees well with Johnson and Tobolsky's value [11] (0·83), whereas Arnett and Peterson [12] obtained 0·63 at 77°.

With αα′-azo-α-methylbutyronitrile and αα′-azo-α-methylvaleronitrile f is 0·82 and 0·87 respectively, showing that the efficiency is nearly constant for all three azonitriles and substitution has little effect on it.

Using a tracer technique, Bevington [13] has concluded that in styrene polymerization the efficiency of azonitriles is independent of the monomer concentration unless the latter is too low. Our work with methyl methacrylate also shows the same constant trend in not too dilute solutions, and f increases only at very high concentration. With αα′-azo-α-methylbutyronitrile in toluene, f is constant over the whole range employed but with other azonitriles the values are scattered. At a particular monomer concentration, however, the efficiency is practically equal in both solvents, implying that the solvent has little effect on the efficiency.

[8] Overberger, O'Shaughnessy, and Shalit, *J. Amer. Chem. Soc.*, 1949, **71**, 2661.
[9] Lewis and Matheson, *J. Amer. Chem. Soc.*, 1949, **71**, 747.
[10] Bawn and Mellish, *Trans. Faraday Soc.*, 1951, **47**, 1216.
[11] Johnson and Tobolsky, *ibid.*, 1952, **74**, 938.
[12] Arnett and Peterson, *ibid.*, p. 2031.
[13] Bevington, *Trans. Faraday Soc.*, 1955, **51**, 1392.

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Though with αα′-azo-α-methylbutyronitrile the efficiency in concentrations of monomer ranging from 50% to 10% remains almost constant (0·50) it is definitely less than that for bulk (0·82).

Chain-transfer Coefficients.—Transfer with initiator (C_I). The general equation for the average degree of polymerization [eqn. (3)] for bulk can be written as

$$(1/\overline{P}) - R_p(\delta^2/M^2) = C_M + C_I(I/M) \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

The plot of the left-hand side against I/M will be linear and C_I can be obtained from the slope, as was done with peroxides.[2a, 14] For our azonitriles the plot was linear but parallel to the abscissa, showing that no transfer occurs. This supports the conclusion that azonitriles do not undergo induced decomposition, the cleavage of the catalyst being unimolecular.

Transfer with monomer (C_M). As C_I is practically zero, a plot of $1/\overline{P}$ against R_p [eqn. (4)] gives C_M from the intercept, as in the determination of δ.

Table 1 gives our results for C_M, being in all cases $1·0 \times 10^{-5}$ at 60°, confirming that obtained by Saha, Nandi, and Palit [2] with benzoyl peroxides, by Nandi and Palit [6f] from hydrogen peroxide-catalysed polymerization of methyl methacrylate, and by Baysal and Tobolsky [6d] with benzoyl peroxide and αα′-azo*iso*butyronitrile, although O'Brien and Gornick [15] obtained a lower value of $0·7 \times 10^{-5}$.

Transfer with solvent (C_S). The suitability of using azonitriles for determining solvent-transfer constants has been examined in systems of few azonitriles with ethyl acetate and toluene. We saw [14,16] that Mayo's method of determining C_S from the plot of $1/\overline{P}$ against S/M is valid where R_p is proportional to M^2. For toluene and ethyl acetate, R_p is proportional to $M^{1·1}$ and M respectively and, as expected, this plot gave values of C_S increasing with the catalyst concentration, as the first column in Table 4 shows.

TABLE 4. *Determination of C_S in the polymerization of methyl methacrylate at 60° (each value the mean from four experiments).*

10^5C_S from slope of $1/\overline{P}$ *vs.* S/M	10^5C_S from slope of $(1/\overline{P}) - R_p(\delta^2/M^2)$ *vs.* S/M
Solvent, toluene; catalyst *A*.	
10^5C_S (uncatalysed, refs. 2*a*, 14, 16) = 2·0.	
3·50	1·75
3·00	1·90
3·00	1·90
2·60	2·05
Average = 1·90	
Solvent, toluene; catalyst *D*.	
6·60	2·00
4·20	2·00
3·50	1·90
2·00	1·40
Average = 1·83	

10^5C_S from slope of $1/\overline{P}$ *vs.* S/M	10^5C_S from slope of $(1/\overline{P}) - R_p(\delta^2/M^2)$ *vs.* S/M
Solvent, toluene; catalyst *B*.	
5·20	2·70
4·80	3·02
3·90	3·10
3·10	2·30
Average = 2·70	
Solvent, ethyl acetate; catalyst *B*.	
10^5C_S (uncatalysed, refs. 2*a*, 14, 16) = 1·30.	
3·10	1·25
2·80	2·00
2·00	1·25
Average = 1·50	

Our modified method of plotting $(1/\overline{P}) - (\delta^2/M^2)R_p$ against S/M, however, gives fairly correct values for C_S as shown in the second column of Table 4, the average value being comparable with those in the literature. Hence these catalysts can be successful in the evaluation of C_S in catalysed systems.

EXPERIMENTAL

Monomer and Solvents.—Quinol-stabilized methyl methacrylate (National Chemical Laboratory) was purified by repeated washing with 5% aqueous sodium hydroxide followed by

[14] Nandi and Palit, Proceedings of International Symposium on Macromolecules, Milan, 1954, published in *Ricerca sci.*, 1954.
[15] O'Brien and Gornick, *J. Amer. Chem. Soc.*, 1955, **77**, 4757.
[16] Palit, Nandi, and Saha, *J. Polymer Sci.*, 1954, **14**, 295.

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water. After being dried ($CaCl_2$) it was fractionally distilled twice, and the fraction of b. p. 100—100·5° collected. The monomer was 98—99% pure (bromine addition method [17]).

" AnalaR " and L. R. samples were purified by the usual methods, dried, and fractionally distilled before use.

Preparation of Azonitriles.—Azonitriles were prepared by Overberger, O'Shaughnessy, and Shalit's method [3] and repeatedly crystallized from absolute ethyl alcohol.

Polymerizations.—The procedure adopted was as previously described.[2, 6f, 16, 18] To exclude oxygen we have taken general precautions, *e.g.*, passing nitrogen through the monomer, degassing the reaction mixtures by vacuum and nitrogen-flushing, etc.

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CALCUTTA—32.

[*Received, April 8th*, 1957.]

[17] Kauffmann and Hartweg, *Ber.*, 1937, **70**, 2554.
[18] Basu, Sen, and Palit, *Proc. Roy. Soc.*, 1950, *A*, **202**, 485.

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3. *The Effect of Temperature on Azonitriles as Initiators in the Polymerization of Styrene.*

By (the late) N. G. SAHA, U. S. NANDI, and SANTI R. PALIT.

Kinetic constants of the polymerization of styrene were studied from 30° to 117°. The rate of polymerization, R_p, is proportional to $I^{0.5}$. The rates of initiation for all the azonitriles are about the same; the corresponding energies of activation and frequency factors have been compared with literature values. The efficiency factor is near 0·6 and is little affected by change of initiator or temperature.

The values of δ, C_M and C_I have been evaluated with six azonitriles and equations are given: $C_I \simeq 0$. The chain-transfer coefficient for toluene has also been determined with one azonitrile; results agree with those in the literature.

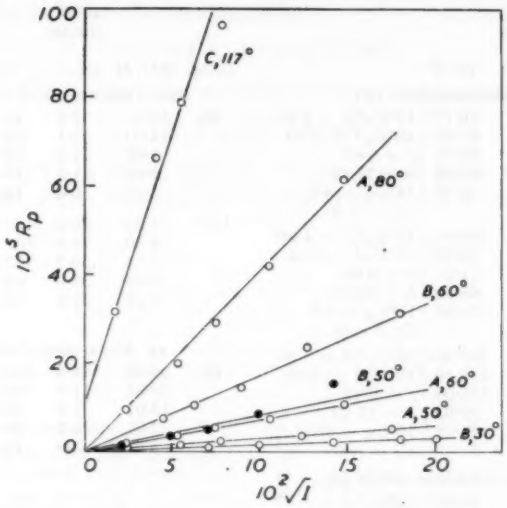
SIX azonitriles, similar to those used in the preceding paper [1] to polymerize methyl methacrylate, have been applied to styrene, with special emphasis on the effect of temperature. The symbols, equations, and methods are those of the preceding paper.[1]

Effect of Initiator Concentration on the Rate of Polymerization.—Fig. 1 shows plots of R_p versus $I^{\frac{1}{2}}$ for the bulk polymerization of styrene over the range 30—117°. They are linear, as with methyl methacrylate [1,2] and styrene with other initiators and may indicate that the termination reaction is of second order.

Evaluation of δ.—We have evaluated δ from the slope of the plot of $1/\bar{P}$ against R_p (Fig. 2) as previously.[1] Results are in Table 1. The temperature variation of δ and hence the corresponding energy of activation $E_p - \frac{1}{2}E_t$ were calculated. Table 2 and Fig. 3 contain our results and values for δ from the literature.[3-9] Our value for $E_p - \frac{1}{2}E_t$ agrees well with most of the literature values, which are about 5 kcal. mole^{-1}, except for one very high value of 19·34 kcal. mole^{-1} (Baysal and Tobolsky [7]). Our value of 28·6 for δ at 60° agrees fairly well with 29·39 by Baysal and Tobolsky [7] and 25·0 by Bonsal *et al.*[6] but Baysal and Tobolsky's [7] value of 122·0 for δ at 47·8° seems to be high. In Fig. 3 the straight-line

[1] Saha, Nandi, and Palit, *J.*, 1956, **85**, 427; and preceding paper.
[2] Nandi and Palit, *J. Polymer Sci.*, 1955, **17**, 65.
[3] Melville and Valentine, *Trans. Faraday Soc.*, 1950, **46**, 210; *Proc. Roy. Soc.*, 1950, *A*, **200**, 337.
[4] Bamford and Dewar, *Proc. Roy. Soc.*, 1948, *A*, **192**, 309.
[5] Burnett, *Trans. Faraday Soc.*, 1950, **46**, 1772.
[6] Bonsal, Valentine, and Melville, *ibid.*, 1952, **48**, 763.
[7] Baysal and Tobolsky, *J. Polymer Sci.*, 1952, **8**, 529.
[8] Matheson, Auer, Bevilacqua, and Hart, *J. Amer. Chem. Soc.*, 1951, **73**, 1700.
[9] Tobolsky and Baysal, *J. Polymer Sci.*, 1953, **11**, 471.

FIG. 1. *Dependence of R_p on catalyst concentration (for catalysts, see Table 1).*



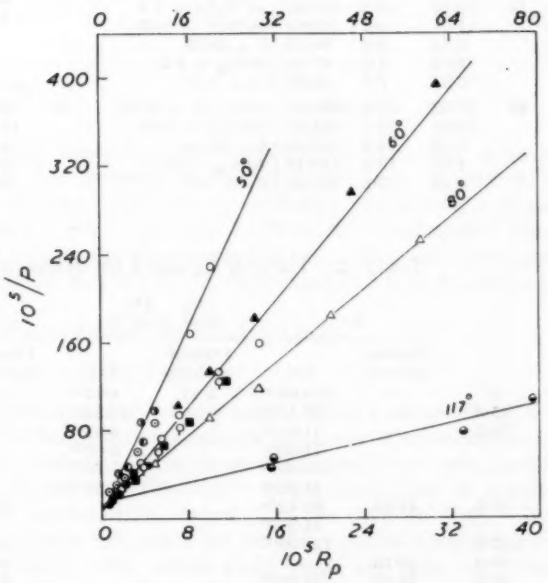


FIG. 2. *Determination of δ at different temperatures (for catalysts, see Table 1).*

○ *A*, 60°; △ *A*, 80°; ⊙ *A*, 50°; ◑ *B*, 50°; ▲ *B*, 60°; ● *C*, 60°; ◒ *C*, 117°; ♀ *D*, 60°; ■ *E*, 60°; ◐ *F*, 50°.

TABLE 1. *Polymerization of styrene in bulk (8·63 moles l.$^{-1}$) in presence of catalysts at different temperatures.*

Temp.	$10^4 I/M$	$10^5/R_p$ (moles l.$^{-1}$ sec.$^{-1}$)	$10^5/\overline{P}$	
		αα′-Azo*iso*butyronitrile (*A*)		
50°	35·29	5·0	86·77	$10^8 R_p^2/I = 8·99$
	17·64	3·4	61·20	$10^6 R_t/I = 2·99$
	7·06	2·1	36·79	$f = 0·60$
	3·53	1·5	31·05	$\delta = 35·15$
	0·71	0·7	15·79	$10^5 C_M = 4·0$
				$C_I = \sim 0$
60	25·64	10·7	133·00	$10^7 R_p^2/I = 4·90$
	12·82	7·2	94·30	$10^5 R_t/I = 1·14$
	6·41	5·6	71·77	$f = 0·66$
	3·21	3·8	48·50	$\delta = 28·51$
	0·64	1·9	28·50	$10^5 C_M = 6·0$
				$C_I = \sim 0$
80	25·64	61·4	252·30	$10^5 R_p^2/I = 1·60$
	12·82	41·9	185·10	$10^4 R_t/I = 6·40$
	6·41	29·0	116·00	$f = 0·41$
	3·21	19·9	90·63	$\delta = 17·29$
	0·64	9·5	47·32	$10^5 C_M = 10·0$
				$C_I = \sim 0$
		αα′-Azo-αγ-dimethylvaleronitrile (*B*)		
30	46·72	2·9	90·63	$10^8 R_p^2/I = 1·77$
	37·32	2·8	73·45	$10^6 R_t/I = 1·06$
	23·36	2·1	65·60	$\delta = 47·26$
	11·68	1·5	50·06	$10^5 C_M = 2·0$
	5·84	0·9	32·30	$C_I = \sim 0$
50	23·36	10·2	228·60	$10^7 R_p^2/I = 6·4$
	11·68	8·2	168·60	$10^5 R_t/I = 2·56$
	5·84	4·9	98·17	$\delta = 38·59$
	2·92	3·6	87·90	$10^5 C_M = 4·0$
	0·58	1·7	40·68	$C_I = \sim 0$
60	37·32	31·0	393·20	$10^7 R_p^2/I = 29·38$
	18·66	23·1	294·80	$10^5 R_t/I = 7·46$
	9·33	14·3	182·20	$\delta = 30·18$
	4·67	10·3	133·40	$10^5 C_M = 6·0$
	2·33	7·2	102·00	$C_I = \sim 0$
		Azo*cyclo*hexane-1 : 1′-dicarbonitrile (*C*)		
60	38·01	2·9	40·43	$10^7 R_p^2/I = 0·24$
	14·00	2·1	29·99	$10^7 R_t/I = 5·35$
	7·00	1·6	21·85	$\delta = 28·63$
	3·50	1·5	16·52	$10^5 C_M = 6·0$
	1·75	0·8	13·06	$C_I = \sim 0$
117	7·00	96·4	130·30	$10^4 R_p^2/I = 1·0$
	3·50	78·9	107·40	$10^4 R_t/I = 2·4$
	1·75	66·2	77·00	$\delta = 9·45$
	0·35	31·6	53·14	$10^5 C_M = 14·0$
	0·18	31·2	45·76	$C_I = \sim 0$
		αα′-Azo-α-methylvaleronitrile (*D*)		
60	56·06	14·6	159·10	$10^7 R_p^2/I = 4·13$
	28·03	11·0	125·00	$10^5 R_t/I = 1·05$
	14·01	7·3	81·66	$f = 0·51$
	7·01	5·3	59·43	$\delta = 28·58$
	3·50	3·9	47·32	$10^5 C_M = 6·0$
				$C_I = \sim 0$
		αα′-Azo-α-methylbutyronitrile (*E*)		
60	48·20	11·3	124·20	$10^7 R_p^2/I = 3·03$
	24·10	8·2	84·14	$10^6 R_t/I = 6·05$
	12·05	5·7	67·54	$f = 0·50$
	6·03	4·2	48·93	$\delta = 27·29$
	3·01	3·1	37·96	$10^5 C_M = 6·0$
				$C_I = \sim 0$
		αα′-Azo-α-methyl*iso*valeronitrile (*F*)		
50	26·04	3·7	69·58	$10^8 R_p^2/I = 6·05$
	13·02	2·6	46·03	$10^5 R_t/I = 1·99$
	5·20	1·6	28·64	$\delta = 35·16$
	2·60	1·2	20·89	$10^5 C_M = 4·10$
	0·52	0·7	14·09	$C_I = \sim 0$

TABLE 2. *Value of C_M and δ for styrene at different temperatures.*

	δ		$E_p - \frac{1}{2}E_t$ (kcal. mole^{-1})		$10^5 C_M$		$E_{tr,M} - E_p$ (kcal. mole^{-1})	
	Present authors	Lit.	Present authors	Lit.	Present authors	Lit.	Present authors	Lit.
0°	—	308·60[6]	4·47	4·87[3]	—	1·1[4]	5·3	7·9[4]
15·0	—	80·32[5]		19·34[7]	—	1·9[5]		7·9[5]
25·0	—	71·61[3]		6·58[6]	—	3·7[4]		
		71·30[3]		5·00[3]		3·2[5]		
		110·80[6]		5·10[4]		1·1[6]		
		61·80[5]		5·35[5]				
30·0	48·93	62·43[3]			2·0	3·2[6]		
		91·37[5]						
47·8	—	122·00[7]			—	—		
50·0	35·15	—			4·0	—		
60·0	28·62	25·00[6]			6·0	6·0[14]		
		36·40[4]						
		29·39[7]						
		34·09[6]						
67·8	—	21·83[7]			—	—		
80·0	19·36	—			10·0	—		
117·0	9·45	—			14·0	—		

plot of log $(1/\delta)$ against $1/T$ fits Baysal and Tobolsky's values at 60° and 67·8° well, but not their value for 47·8°. This may account for their high value of $E_p - \frac{1}{2}E_t$.

We conclude that δ can best be represented by

$$\delta = 9{\cdot}4 \times 10^{-3} \exp(4{\cdot}4/RT)$$

Rate of Initiation (R_i/I).—As in the preceding paper we determined R_i/I from

$$R_i/I = 2\delta^2 R_p^2/IM^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

by using values of R_p^2/I and δ from Table 1. In the present paper R_i/I was determined for the six azonitriles within temperatures ranging from 30° to 117° and results are shown

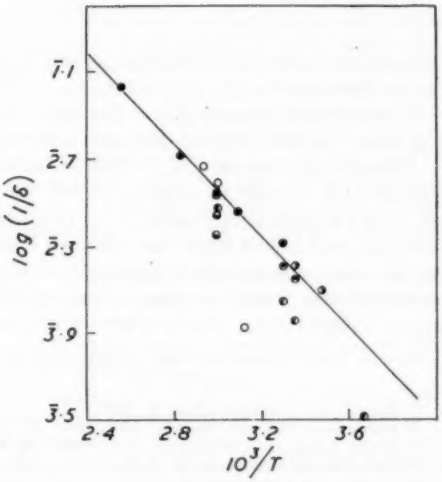


FIG. 3. *Effect of temperature on* δ.

● Present authors, ◓ Melville and Valentine,[3] ◑ Burnett,[5] ◒ Bamford and Dewar,[4] ⚲ Bonsal, Valentine, and Melville,[6] ○ Baysal and Tobolsky,[7] ◐ Matheson *et al.*[8]

therein. For αα′-azo*iso*butyronitrile, azo*cyclo*hexane-1 : 1′-dicarbonitrile, and αα′-azo-αγ-dimethylvaleronitrile R_i/I can be represented by $9{\cdot}2 \times 10^{13} \exp(-28{\cdot}5/RT)$, $6{\cdot}82 \times 10^{11} \exp(-27{\cdot}6/RT)$, and $8{\cdot}89 \times 10^{14} \exp(-28{\cdot}9/RT)$ respectively. These results can be compared with $R_i/I = 6{\cdot}3 \times 10^{13} \exp(-28{\cdot}48/RT)$ recalculated from Tobolsky and Baysal's [9] compiled data by the least-square method. They also calculated the E and A factors for several peroxides and find that E varies from 25·5 to 31·5 kcal./mole and A from 10^{11} to 10^{16}.

Efficiency, f.—The efficiency of the azonitriles was calculated from

$$f = (R_i/I)/(2kd)$$

kd for benzene as reported by Overberger *et al.*[10] being used. Table 1 shows that f lies between 0·51 and 0·66, which demonstrates the approximate constancy of the efficiency of different azonitriles. This further confirms our previous conclusion [1] that substitution has little effect on efficiency. Johnson and Tobolsky,[11] in polymerization of styrene initiated by azo*cyclo*hexane-1 : 1′-dicarbonitrile, found f to be 0·64 at 80·3°. The efficiency of azo*iso*butyronitrile has been calculated by various workers using different procedures and values vary from 0·81 to 0·66, within which range our value lies. The efficiency is almost independent of temperature (Table 1).

Monomer Transfer (C_M).—Using the same method as for δ, we determined C_M, as represented in Fig. 2 and Table 1.

[10] Overberger, Fram, and Alfrey, *J. Polymer Sci.*, 1951, **6**, 539.
[11] Johnson and Tobolsky, *J. Amer. Chem. Soc.*, 1952, **74**, 938.

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Our value at 60° agrees well with those of Baysal and Tobolsky [7] and Mayo *et al.*[14] For lower temperatures Bamford and Dewar [4] and Burnett [5] give values slightly higher than ours. The temperature variation of C_M and hence the corresponding energy of activation $E_{tr,M} - E_p$ is 5·30 kcal. mole^{-1}; Bamford and Dewar [4] and Burnett [5] report

TABLE 3. *Determination of C_S for toluene in polymerization of styrene at 60° initiated by αα′-azoisobutyronitrile (uncatalysed value 2·00).*

No. of expts.	$1/\overline{P}$ *vs.* S/M	10^4C_S from slope of $\{(1/\overline{P}) - (\delta^2/M^2)R_p\}$ *vs.* S/M
3	9·0	2·2
3	7·5	2·1
3	4·3	2·1
4	2·0	2·1
		Average = 2·1

7·9 but their values were obtained at two temperatures only. The most probable value of C_M, *i.e.* the ratio $k_{tr,M}/k_p$, is given by $C_M = 16{\cdot}4 \times 10^{-2} \exp(-5{\cdot}30/RT)$.

Transfer with Initiator (C_I).—The slope of $[(1/\overline{P}) - (\delta^2/M^2)R_p]$ against I/M, *i.e.*, C_I, is near zero. As with methyl methacrylate,[1] no induced decomposition was observed.

Transfer with Solvent (C_S).—With αα′-azoisobutyronitrile as initiator the chain-transfer constant for toluene in styrene at 60° has been verified with an initiator range of $7{\cdot}0 \times 10^{-4}$ to $14{\cdot}0 \times 10^{-3}$ moles l.$^{-1}$. In all cases C_S obtained from the slope of $1/\overline{P}$ *versus* S/M plots was higher than that obtained from the results for uncatalysed polymerization, but by using our modified method [15] of plotting $\{(1/\overline{P}) - R_p(\delta^2/M^2)\}$ against S/M fair agreement was found between values obtained from catalysed and uncatalysed experiments. Some typical results briefly summarised in Table 3 illustrate the point.

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CALCUTTA—32.

[*Received, April 8th*, 1957.]

[12] Arnett and Peterson, *ibid.*, p. 2031.
[13] Hammond, Sen, and Boozer, *ibid.*, 1955, **77**, 3244.
[14] Mayo, Gregg, and Matheson, *ibid.*, 1951, **73**, 1671.
[15] Palit, Nandi, and Saha, *J. Polymer Sci.*, 1954, **14**, 295.

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4. *Molecular Polarisability. The Molar Kerr Constants and Dipole Moments of* spiro- *and Other Derivatives of Pentaerythritol.*

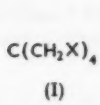
By (MRS.) C. G. LE FÈVRE, R. J. W. LE FÈVRE, and M. R. SMITH.

Pentaerythritol tetrachloride, tetrabromide, and tetra-acetate, and the dimethylene- and dibenzylidene-derivatives of pentaerythritol have been examined as solutes in carbon tetrachloride. In each case the total polarisation exceeds the molecular refraction. Reasons are given for viewing the moments of the first three compounds as " apparent," and ascribable to " vibration polarisation," a phenomenon which the flexible tetra-acetate exhibits in an unusual degree. Structures of the type $C(CH_2X)_4$ with the four X groups at the corners of a square plane containing the central carbon atom are reconcilable with all the results now found. In dimethylene-pentaerythritol the two *spiro*-1 : 3-dioxan rings may have " boat " or " chair " conformations. The molar Kerr constant, in conjunction with other properties, indicates as correct a " chair–chair " structure, rather than one in which the rings are " boat–boat " or " boat–chair."

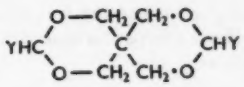
THE three pentaerythritol derivatives (I; X = Cl, Br, or OAc) were examined to obtain information on tetrahedrally symmetric structures additional to that available to Le Fèvre, Le Fèvre, and Narayana Rao [1] for the simple cases CH_4, CCl_4, and CBr_4. Subsequently,

[1] Le Fèvre, Le Fèvre, and Narayana Rao, *J.*, 1956, 708.

the two compounds (II; Y = H or Ph) were added; the first was subjected to conformational analysis through the polarisability ellipsoids [2] recently computed [3] for C–C and C–O bonds. Dielectric polarisations and relaxation times were also determined.



(I)



(II)

Experimental

Materials.—Pentaerythritol tetrachloride was obtained from pentaerythritol and thionyl chloride in presence of pyridine.[4] (The method involving phosphorus trichloride [5] appeared to be inferior.) It crystallised from aqueous ethanol as white leaflets, m. p. 96·0—97·5° (lit. 97°). Pentaerythritol tetrabromide, prepared as in ref. 5, was twice crystallised from 95% ethanol from 20° to −10°, and had m. p. 157·6—158·2° (lit., 163°,[5] 158° [6]). Pentaerythritol tetraacetate,[7] from light petroleum, had m. p. 81—82°. *OO′-O″O‴*-Dimethylenepentaerythritol (II; Y = H), made as by Read,[8] formed white crystals, m. p. 49—51° (lit., 50° [8, 9]), and the dibenzylidene analogue [8, 9] formed white plates, m. p. 156·5—157° (lit., 160°), from chloroform. Tetranitromethane (" pure " commercial sample) was steam-distilled, dried (Na_2SO_4), then partially frozen, and the solid separated; after melting it was redried ($MgSO_4$), filtered, and stored in a well-stoppered flask; m. p. 13°.

Carbon tetrachloride. This was used as solvent throughout all the measurements. It was from the " sulphur-free " bulk supply noted in ref. 10. It was stored over calcium chloride and filtered immediately before use.

Dielectric Polarisations.—These were determined by standard procedures,[11] except that for capacity comparisons the circuit described in ref. 12 was used.

Relaxation Times.—The equipment was that described by Le Fèvre and Sullivan,[13] and Chau, Le Fèvre, and Tardif.[14] The formulæ by which the relaxation time τ of a solute is extracted from the observed Q factors are given in ref. 13.

Electric Double Refractions.—Le Fèvre and Le Fèvre's [2, 15] apparatus was used, modified only by the insertion of a " Scalamp " electrostatic voltmeter in parallel with the cell leads to obtain higher accuracy in the voltage readings. Refractive indexes were taken on an Abbé refractometer.

Symbols.—These have significances as follow (suffixes 1, 2, and 12 being applied to indicate respectively solvent, solute, and solution): w, weight fractions; ε, dielectric constants; d, densities; n, refractive indexes; M, molecular weights; R, molecular refractions; p, specific polarisations; $_\infty P$, total polarisations at infinite dilution; μ, dipole moments; Δf, the widths (in frequency units, mc./sec.) at half-heights of the resonance curves involved in measurements of loss tangents (here called tan ϕ—an inconsistency with refs. 13 and 14 but necessary—since the letter δ is also used in another connection) and relaxation times τ; $\Delta \tan \phi$, the differences between the loss tangents of solutions and solvent; ψ is $(\Delta \tan \phi)/w_2$; B denotes Kerr constants; ΔB, the changes in Kerr constant from solvent to solutions; $_sK$, specific Kerr constants; $_\infty(_mK)$, molar Kerr constants at infinite dilution; α, β, γ, δ, are quantities obtained by

[2] Le Fèvre and Le Fèvre, *Rev. Pure Appl. Chem.*, 1955, **5**, 261.
[3] *Idem*, *J.*, 1956, 3549.
[4] Mooradian and Cloke, *J. Amer. Chem. Soc.*, 1945, **67**, 942.
[5] Schurink, " Organic Syntheses," Coll. Vol. II, 476.
[6] Ebert, Eisenschitz, and Hartel, *Z. phys. Chem.*, 1928, *B*, **1**, 94.
[7] Orthner and Freyss, *Annalen*, 1930, **484**, 131.
[8] Read, *J.*, 1912, **101**, 2090.
[9] Schulz and Tollens, *Annalen*, 1896, **289**, 28.
[10] Le Fèvre and Le Fèvre, *J.*, 1954, 1577.
[11] Le Fèvre, " Dipole Moments," Methuen, 3rd Edn., 1953, Chap. II.
[12] Buckingham, Chau, Freeman, Le Fèvre, Narayana Rao, and Tardif, *J.*, 1956, 1405.
[13] Le Fèvre and Sullivan, *J.*, 1954, 2873.
[14] Chau, Le Fèvre, and Tardif, *J.*, 1957, 2293.
[15] Le Fèvre and Le Fèvre, *J.*, 1953, 4041.

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taking $\varepsilon_{12} = \varepsilon_1(1 + \alpha w_2)$, $d_{12} = d_1(1 + \beta w_2)$, $n_{12} = n_1(1 + \gamma w_2)$, and $B_{12} = B_1(1 + \delta w_2)$. Then:

$$_{\infty}P_2 = [p_1(1 - \beta) + C\alpha\varepsilon_2]M_2$$

and

$$_{\infty}(_{\mathrm{m}}K_2) = {}_{\mathrm{s}}K_1(1 - \beta + \gamma + \delta - H\gamma - J\alpha\varepsilon_2)M_2$$

where C, H, and J are constants for the solvent (see refs. 10 and 11 for further details).

Tables 1—4 record experimental observations, from which the results presented in Tables 5 and 6 are deduced.

TABLE 1. *Dielectric polarisation measurements in carbon tetrachloride at* 25° ($\varepsilon_1 = 2{\cdot}2270$; $d_1 = 1{\cdot}58454$)

10^5w_2	ε_{12}	d_{12}	10^5w_2	ε_{12}	d_{12}	10^5w_2	ε_{12}	d_{12}	10^5w_2	ε_{12}	d_{12}
Pentaerythritol tetrachloride						*Pentaerythritol tetra-acetate*					
526	2·2293	1·58365	1287	2·2317	1·58260	680	2·2501	1·58067	1080	2·2637	1·57821
568	2·2294	1·58354	1298	2·2339	—	864	2·2567	1·57946	1333	2·2729	1·57716
767	2·2322	1·58328	2341	—	1·58054	942	2·2578	1·57928			
whence $\Sigma\Delta\varepsilon/\Sigma w_2 = 0{\cdot}484$, $\Sigma\Delta d/\Sigma w_2 = -0{\cdot}165$						whence $\Sigma\Delta\varepsilon/\Sigma w_2 = 3{\cdot}41$, $\Sigma\Delta d/\Sigma w_2 = -0{\cdot}564$					
Pentaerythritol tetrabromide						*Dimethylenepentaerythritol* (II; Y = H)					
585	2·2302	1·58782	1270	2·2344	1·59137	336	2·2564	1·58316	878	2·3038	1·58106
754	2·2313	1·58894	1521	2·2353	1·59276	750	2·2918	1·58152	1068	2·3196	1·58008
1238	2·2341	1·59130	1602	2·2361	1·59348	828	2·2978	1·58109	1378	2·3462	1·57848
whence $\Sigma\Delta\varepsilon/\Sigma w_2 = 0{\cdot}565$, $\Sigma\Delta d/\Sigma w_2 = 0{\cdot}551$						whence $\Sigma\Delta\varepsilon/\Sigma w_2 = 8{\cdot}66$, $\Sigma\Delta d/\Sigma w_2 = -0{\cdot}417$					
Dibenzylidenepentaerythritol (II; Y = Ph)						*Tetranitromethane*					
386	2·2416	1·58264	775	2·2570	1·58035	968	2·2285	1·58454	2139	2·2299	1·58454
441	2·2447	1·58212	890	2·2637	1·57926	2005	2·2290	—	2240	2·2296	—
564	2·2488	1·58168				whence $\Sigma\Delta\varepsilon/\Sigma w_2 = 0{\cdot}122$, $\Sigma\Delta d/\Sigma w_2 = ca.\ 0$					
whence $\Sigma\Delta\varepsilon/\Sigma w_2 = 3{\cdot}95_3$, $\Sigma\Delta d/\Sigma w_2 = -0{\cdot}545$											

TABLE 2. *Refractions* (Na *light*) *at* 25°.

Solute	10^5w_2	n_{D}	γn	Solute	10^5w_2	n_{D}	γn
—	0	1·4575	—	(II; Y = Ph) ...	543	1·4583	0·1473
$C(CH_2Cl)_4$	3976	1·4602	0·0679	$C(NO_3)_4$	859	1·4572	−0·0348
$C(CH_2Br)_4$	2999	1·4614	0·1302	,, ...	1482	1·4570	
$C(CH_2OAc)_4$	2198	1·4574	−0·0045	,, ...	2287	1·4567	
(II; Y = H) ...	4527	1·4589	0·0309	,, ...	2834	1·4565	

TABLE 3. *Loss tangents for solutions in carbon tetrachloride.*

At 15°			At 19°		
Pentaerythritol tetra-acetate					
0	1·79	—	0	1·93	—
1015	2·27	1·91	811	2·15	0·88
1333	2·33	2·15	1063	2·24	1·24
			0	1·83	—
			2248	2·65	3·27
Dimethylenepentaerythritol, at 17°					
0	1·70	—	1378	3·91	8·81
829	3·13	5·70			

TABLE 4. *Electric double refractions of solutions in carbon tetrachloride.*

Pentaerythritol tetrachloride						*Pentaerythritol tetrabromide*				
10^5w_2 ...	346	515	1169	1653		690	820	829	1340	1490
$10^7\Delta B$ ...	*ca.* 0	*ca.* 0	*ca.* 0	*ca.* 0		*ca.* 0	*ca.* 0	*ca.* 0	*ca.* 0	*ca.* 0
Pentaerythritol tetra-acetate						*Dimethylenepentaerythritol*				
10^5w_2 ...	272	440	892	1108	1544	527	742	992	1811	1980
$10^7\Delta B$ ...	0·001	0·002	0·003	0·004	0·005	−0·006	−0·011	−0·011	−0·028	−0·033
whence $\Sigma(w_2 \cdot \Delta B)/\Sigma w_2 = 0{\cdot}342 \times 10^{-7}$						whence $10^7\Delta B = -0{\cdot}9450w_2 - 35w_2^2$				
Dibenzylidenepentaerythritol						*Tetranitromethane*				
10^5w_2 ...	167	246	248	338		859	1758	1860	2084	2834
$10^7\Delta B$ ...	−0·004	−0·007	−0·007	−0·009		0·001	0·004	0·004	0·005	0·008
whence $10^7\Delta B = -2{\cdot}656w_2 - 21w_2^2$						whence $10^7\Delta B = 0{\cdot}074w_2 + 8{\cdot}3w_2^2$				

TABLE 5. *Calculations of molar Kerr constants at infinite dilution.*

Solute *	$\alpha\varepsilon_1$	β	γ	δ	M_2	$_\infty({}_mK_2) \times 10^{12}$
P.E. tetrachloride	0·484	−0·104	0·047	*ca.* 0	209·9	1·30
P.E. tetrabromide	0·565	0·348	0·089	*ca.* 0	387·8	0·8$_5$
P.E. tetra-acetate	3·41	−0·356	−0·003	4·88	304·3	10·5
Dimethylene-P.E.	8·66	−0·263	0·021	−13·5	160·2	−19·6 †
Dibenzylidene-P.E. ...	3·95	−0·344	0·101	−37·9	312·3	−90·2 †
Tetranitromethane ...	0·122	*ca.* 0	−0·024	1·06	196·0	2·9$_8$

* P.E. = " Pentaerythritol."
† These values amend the (higher) preliminary results included in Table 7 of ref. 2.

TABLE 6. *Calculations of dipole moments and relaxation times.*

Solute	$_\infty P_2$ (c.c.) *	R_D (c.c.)	μ (D) †	ψ	$\tau \times 10^{12}$ (sec.)
$C_5H_8Cl_4$	53·2	44·5	0·65	*ca.* 0	—
$C_5H_8Br_4$	69·5	59·9	0·68	*ca.* 0	—
$C_{12}H_{20}O_8$	185·6	70·5	2·3$_7$	0·146	5
$C_7H_{12}O_4$	184·1	36·4	2·6$_3$	0·658	8·5
$C_{19}H_{20}O_4$	207·7	86·9	2·4$_3$	—	—
$C(NO_3)_4$	38·4$_3$	31·5	0·58	*ca.* 0	—

* Using values of $\alpha\varepsilon_1$, β, and M_2 from Table 5.
† *I.e.*, apparent moment obtained by taking $_DP = R_D$.

TABLE 7. *Previously recorded polarisations and dipole moments.*

	Temp.	Solvent	$_\infty P_2$ (c.c.)	μ (D) quoted	Ref.
$C(CH_2Cl)_4$ ...	—	C_6H_6	52	<0·2	6, 16
	No measurements given			0	17
$C(CH_2OAc)_4$	—	C_6H_6	250	2·6	16
	—	CCl_4	214	—	6
	25°	C_6H_6	140	1·9	17
	22	C_6H_6	175·2	2·18	7
	Molecular beam method		*ca.* 3		18
$C(CH_2Br)_4$ ...	—	C_6H_6	62	*ca.* 0	6
	—	CCl_4	63	*ca.* 0	6
	25°	C_6H_6	56	0	17
	Molecular beam method			0	18
$C(NO_3)_4$	25	C_6H_6	32·5	<0·2	17
	25	CCl_4	36·24	0·19	19
	25	C_6H_6	37·5	0·48	19
	25	CCl_4	41·7	0·71	20
	81·8	gas	38·6	—	21

DISCUSSION

Previous measurements (Table 7) of the polarisations at infinite dilution of pentaerythritol tetrachloride, tetrabromide, and tetra-acetate disagree among themselves. The values now recorded for $C(CH_2Cl)_4$ and $C(CH_2Br)_4$ differ by about the same amount as do the two molecular refractions (*ca.* 16 c.c.), and if R_D were the correct distortion polarisation, would correspond to the apparent moments shown in Table 6. However, the absence of dielectric loss with solutions in carbon tetrachloride, and the smallness of the observed molar Kerr constant (Table 5), are consistent with a near-isotropy and non-polarity of both these molecules, so that the excesses of $_\infty P_2$ over R_D may be attributed to atomic polarisation of the type explained by Coop and Sutton.[21] There seems no case today for considering early suggestions [22] that the central carbon atom has the valency configuration of a quadrilaterally based pyramid. Wagner and Dengel,[23] and de Laszlo,[24] supposed

[16] Ebert and Hartel, *Naturwiss.*, 1927, **15**, 669.
[17] Williams, *Physikal. Z.*, 1928, **29**, 271, 683; *J. Amer. Chem. Soc.*, 1928, **50**, 2350.
[18] Estermann and Wohlwill, *Z. phys. Chem.*, 1933, *B*, **20**, 195.
[19] Weissberger and Sängewald, *Ber.*, 1932, **65**, 701.
[20] Lewis and Smyth, *J. Amer. Chem. Soc.*, 1939, **61**, 3067.
[21] Coop and Sutton, *J.*, 1938, 1269.
[22] Guillemin, *Ann. Physik*, 1926, **81**, 173; Hund, *Leipz. Vortr.*, 1929, 78; Henri, *Chem. Rev.*, 1927, **4**, 189; Cabannes *et al.*, *J. Phys. Radium*, 1925, **6**, 182; *Compt. rend.*, 1926, **182**, 885; Cooley, *Astrophys. J.*, 1925, **62**, 73; Weissenberg, *Ber.*, 1926, **59**, 1526; *Z. Kryst.*, 1925, **62**, 12; Mark and Weissenberg, *Z. Physik*, 1923, **17**, 301; Huggins and Hendricks, *J. Amer. Chem. Soc.*, 1926, **48**, 164; Gerstacker *et al.*, *Z. Kryst.*, 1928, **66**, 355; Mark and Susich, *ibid.*, 1929, **69**, 105; Nitta, *Bull. Chem. Soc. Japan*, 1927, **1**, 62; Schleede, *Z. anorg. Chem.*, 1928, **168**, 313; **172**, 121; Moller and Reis, *Z. Kryst.*, 1928, **68**, 385; Goodwin and Hardy, *Proc. Roy. Soc.*, 1938, *A*, **164**, 369; Booth and Llewellyn, *J.*, 1947, 837.
[23] Wagner and Dengel, *Z. phys. Chem.*, 1932, *B*, **16**, 382.
[24] De Laszlo, *Compt. rend.*, 1934, **198**, 2235.

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that the four halogen atoms lay at the corners of a square plane containing the central carbon atom; this conformation was criticised by Hassel and Stromme,[25] who however did not advance any specific alternative. Llewellyn, Cox, and Goodwin [26] have found the four hydroxyl groups in pentaerythritol itself to be similarly situated, while Bientema *et al.*[27] explicitly describe the structure of pentaerythritol tetraphenyl ether as having the central carbon surrounded by four oxygen atoms forming a square horizontal plane with two of the other carbon atoms of the pentaerythritol above it and the other two below it.

Such conformations for the three molecules $C(CH_2X)_4$ are reconcilable with present measurements. First, take the cases where X = Cl or Br. Let b_1 and b_2 act respectively along the two (perpendicular) XX lines, and assume that the angles XCC and CCC have the common value θ; obviously $b_1 = b_2$. Then, by writing b_1 and b_3 in terms of the link polarisabilities [2,3] of the C–C and C–X bonds, and subtracting, we obtain:

$$b_1 - b_3 = 2(\sin^2 \tfrac{1}{2}\theta - 2\cos^2 \tfrac{1}{2}\theta)(b_L^{CX} + b_L^{CC}) + 2(1 + \cos^2 \tfrac{1}{2}\theta - 2\sin^2 \tfrac{1}{2}\theta)(b_T^{CX} + b_T^{CC})$$

It is seen that $b_1 - b_3$ is zero when θ is the tetrahedral angle—a situation which cannot be far from the truth. Since ${}_mK$ contains $(b_1 - b_3)^2$, the observation that $C(CH_2Cl)_4$ and $C(CH_2Br)_4$ have very small values of ${}_\infty({}_mK_2)$ is therefore consistent with the molecular structures proposed in refs. 23 and 24.

For pentaerythritol tetra-acetate Goodwin and Hardy [22] have suggested that the acetate units are planar, that each set of C–C–O–C–(C)–C–O–C–C atoms is a flat zig-zag, and that all angles between single bonds in the molecule are tetrahedral within experimental error. Let the polarisability axes be $b_1 = b_2$ along the O–O directions, with b_3 acting at right angles to them through the central carbon atom (C). The difference $b_1 - b_2$ then follows as:

$$+ 4(\sin^2 \tfrac{1}{2}\theta - 2\cos^2 \tfrac{1}{2}\theta)(b_L^{CC} + b_L^{C-O}) + 4(\cos^2 \tfrac{1}{2}\theta - 2\sin^2 \tfrac{1}{2}\theta + 1)(b_T^{CC} + b_T^{C-O}) + 2(b_T^{C=O} + b_V^{C=O} - 2b_L^{C=O})$$

so that the molar Kerr constant found should largely depend on the polarisabilities of the ketonic groups. By using values previously reported [3] for C=O, namely, $b_L^{C=O} = 0{\cdot}236$, $b_T^{C=O} = 0{\cdot}139$, and $b_V^{C=O} = 0{\cdot}025$ (all $\times 10^{-23}$ c.c.), $b_1 - b_3$ is found to be $-0{\cdot}616 \times 10^{-23}$, and that part of ${}_\infty({}_mK_2)$ due to the "anisotropy term" emerges as $45{\cdot}2 \times 10^{-12}$ (the ratio ${}_DP/{}_EP$ being 186/71, see Table 6). Since the observed ${}_\infty({}_mK_2)$ is $10{\cdot}5 \times 10^{-12}$, a "dipole term" corresponding to $-34{\cdot}7 \times 10^{-12}$ is also required; a resultant dipole moment of 0·714 D, effective along the b_3 direction, will provide it. The "apparent" moment listed in Table 6 leads to a highly negative value of ${}_\infty({}_mK_2)$, *viz.*, -337×10^{-12}, which is in disagreement with the fact. We conclude therefore that pentaerythritol tetra-acetate exhibits vibration polarisation [28] to a more marked degree than do the related pentaerythritol tetrahalides.

Examination of Catalan models of the three molecules mentioned shows the four CH_2X groups locked in a way that mutually prevents rotations around the C–C bonds. Franklin [29] has noted that "free rotation" should produce apparent moments of 2·6—2·8 D for $C(CH_2Cl)_4$ and $C(CH_2Br)_4$ but that dipole–dipole interactions (equivalent approximately to kT) combined with steric hindrances tend to exclude configurations having large moments. The tetra-acetate, however, compared with, *e.g.*, the tetrabromide, carries its polar C=O groups *ca.* 1 Å farther out from the central carbon than does the tetrabromide its C–Br dipoles (cf. refs. 23, 24), so that not only have the $CO{\cdot}CH_3$ units more room in which to rotate about the C–O axis, but dipole–dipole forces are relatively less

[25] Hassel and Stromme, *Z. phys. Chem.*, 1938, *B*, **38**, 349.
[26] Llewellyn, Cox, and Goodwin, *J.*, 1937, 883.
[27] Beintema, Terpstra, and van Weerden, *Rec. Trav. chim.*, 1935, **54**, 627.
[28] Sutton, *Ann. Reports*, 1940, **37**, 57.
[29] Franklin, *J. Amer. Chem. Soc.*, 1951, **73**, 3512.

powerful. In the equations written [21, 28, 30, 31] for atomic (or vibration) polarisation, ${}_{A}P$ is always shown as inversely dependent on the force constants of the various deformations caused by the application of an electric field to a molecule, and especially to the more flexibly held polar bonds thereof. In the present instance the deformation involved is a twisting of $CO{\cdot}CH_3$ about its C–O axis. The appropriate torsional force constant is unknown but is likely to be small compared with the bending force constants usually considered hitherto in this type of problem. Qualitatively, therefore, two consequences seem obvious: (*a*) it is possible for the tetra-acetate to have a large ${}_{A}P$, and (*b*) the structure is such [32, 33] that " segment orientation " can occur, so that the raising (Table 3) of the loss tangent of carbon tetrachloride by this solute is not unexpected. Incidentally, inspection of models indicates that the C–Br links in $C(CH_2Br)_4$ are more confined sterically than are the corresponding bonds in $C(CH_2Cl)_4$. By the argument used in ref. 1, therefore, that the ${}_{m}K$ of the chloro-compound exceeds that of the bromo-derivative, is understandable; that both should be less than the ${}_{m}K$ of tetranitromethane may be due to the greater link polarities associated with the $C(NO_2)_4$ structure than with those of $C(CH_2Cl)_4$ and $C(CH_2Br)_4$.

FIG. 1.

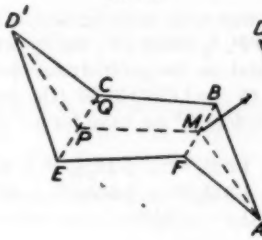
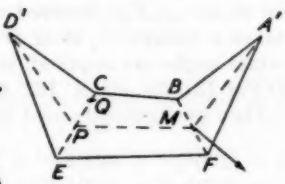


FIG. 2.



The dimethylene- and dibenzylidene-*spiro*-derivatives of pentaerythritol (II) are characterised by having negative molar Kerr constants (Table 5). Their dipole moments are here reported for the first time, although the related condensation product from acetone has been studied by Orthner and Freyss,[7] who found $\mu = 2{\cdot}26$ D. These authors discussed their compound in terms of " boat " and " chair " conformations of the two heterocyclic rings, considering that 36 different arrangements of the whole structure were theoretically possible, so that only those formulæ requiring $\mu = 0$ could be eliminated. The question was left at that stage.

We have attempted an analysis of the moments now obtained (for the *spiro*-compounds) by regarding them as resultants of two components, having mutual orientations depending on the conformations adopted by each of the 1 : 3-dioxan rings, joined by sharing carbon atom 5 in common. It is first necessary to establish the moment (magnitude and direction) appropriate for the " chair " and " boat " versions of 1 : 3-dioxan; the following bond lengths (Å) and valency angles have been assumed: [34] C–C, 1·54; C–O 1·43; $\angle CCC = \angle CCO = \angle OCO = 109°28'$, $\angle COC = 111°$. The moment of the C–O–C bond pair has been taken as that of dimethyl ether,[35] *viz.*, 1·25 D. In Figs. 1 and 2, *D'*, *C*, *A'* and *E* mark the centres of carbon atoms, and *B* and *F* those of the oxygen atoms. The *spiro*-atom is *D'*. In both cases the resultant moment is $1{\cdot}86_5$ D, lying in the planes of the triangles *D'PM* (*P* and *M* being the mid-points of *CE* and *BF*, respectively), and acting in the " chair "

[30] Le Fèvre and Rao, *Aust. J. Chem.*, 1954, **7**, 155; 1955, **8**, 39.
[31] Freeman, Le Fèvre, Rao, and Ross, *J.*, 1955, 3840.
[32] Smyth, " Dielectric Behaviour and Structure," McGraw-Hill, New York, Toronto, London, 1955, p. 111.
[33] Davies, *Quart. Reviews*, 1954, **8**, 250.
[34] Allen and Sutton, *Acta Cryst.*, 1950, **3**, 46.
[35] Barclay and Le Fèvre, *J.*, 1952, 1643.

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and " boat " forms at inclinations to $D'P$ of 92° 15′ and 171° 31′. It is noteworthy that Otto [36] has determined the dipole moments of several 1 : 3-dioxans and found values of the order of that just calculated (*e.g.*, 2-methyl-1 : 3-dioxan has $\mu = 1{\cdot}89$ D).

The moments of different forms of dimethylenepentaerythritol now follow straightforwardly since in (II) the lines $D'P$ for each constituent ring are collinear and the planes of the triangles $D'CE$ are perpendicular about their $PD'D'P$ axis. If the *spiro*-atom D' is at the origin of Cartesian co-ordinates $0z$, $0y$, and $0z$ and the disposition of (II) is defined by the triangles $D'CE$ lying in the planes $y = 0$ and $z = 0$, respectively, then we have for three configurations of (II; Y = H) the following results:

Configuration:	Double " chair "	Double " boat "	" Chair–boat "
Resultant moment (D)	2·66	0·39	$2{\cdot}76_5$
$\mu_{resultant}$ and $0x$ direction	90°	90°	46° 5′
" $0y$ "	45°	45°	48° 14′
" $0z$ "	45°	45°	47° 37′

Table 6 gives the observed moment of dimethylenepentaerythritol as $2{\cdot}6_9$ D—a value incompatible with a double " boat " configuration, but which does not assist decision between the other two possibilities.

The significance of the ${}_{\infty}({}_{m}K_2)$ observed was next investigated. The polarisabilities of each ring were taken as follows: b_1 along $D'P$, b_2 along EC, and b_3 perpendicular to $D'P$ and EC at P. Certain angles are required, and on the geometrical specifications already given these are: $D'PM$ 131° 53′, PMA' 122° 13′, and CBQ 3° 36′ (the position of Q is such that $PQ = MB$). Then by arguments used before [2,3] we have for a " chair " ring:

$$b_1 = (2/3)b_L^{CC} + (4/3)b_T^{CC} + 1{\cdot}53b_L^{CC} + 2{\cdot}46_5b_T^{CC} + 8b^{CH}$$
$$b_2 = (4/3)b_L^{CC} + (2/3)b_T^{CC} + 1{\cdot}34b_L^{CC} + 2{\cdot}66b_T^{CC} + 8b^{CH}$$
$$b_3 = 2b_T^{CC} + 1{\cdot}12b_L^{CC} + 2{\cdot}88b_T^{CC} + 8b^{CH}$$

and for a " boat " ring:

$$b_1^1 = (2/3)b_L^{CC} + (4/3)b_T^{CC} + 0{\cdot}938b_L^{CC} + 3{\cdot}06b_T^{CC} + 8b^{CH}$$
$$b_2^1 \text{ as for } b_2 \text{ " chair "}$$
$$b_3^1 = 2b_T^{CC} + 1{\cdot}72b_L^{CC} + 2{\cdot}28b_T^{CC}$$

From these data the semi-axes for a double " chair " dimethylenepentaerythritol (b_1^{DMP} b_2^{DMP} and b_3^{DMP}, with b_1^{DMP} parallel to $\mu_{resultant}$, and b_2^{DMP} parallel to $PD'D'P$ in the *spiro*-molecule emerge as:

$$b_1^{DMP} = b_2 + b_3 - 4b^{CH}$$
$$b_2^{DMP} = 2b_1 - 4b^{CH}$$
$$b_3^{DMP} = b_2 + b^3 - 4b^{CH}$$

so that:

$$(b_1 - b_2)^{DMP} = -0{\cdot}6048(b_L^{C-O} - b_T^{C-O})$$

Introduction of the value $b_L^{C-O} = 0{\cdot}081 \times 10^{-23}$ and $b_T^{C-O} = 0{\cdot}039 \times 10^{-23}$, previously [3] deduced from paraldehyde, gives $(b_1 - b_2)^{DMP} = -0{\cdot}0254 \times 10^{-23}$, whence $\theta_1 = 0{\cdot}0077 \times 10^{-35}$ and $\theta_2 = -2{\cdot}413 \times 10^{-35}$; the calculated molar Kerr constant is therefore $-10{\cdot}1 \times 10^{-12}$. This value, based on an oxygen angle of 111°, has the correct algebraic sign and order of magnitude but is *ca.* 10 units from the ${}_{\infty}({}_{m}K_2)$ observed.

Accordingly, it is of interest to derive ${}_{\infty}({}_{m}K_2)$ by adopting the polarisabilities of the C–O bond obtained from different compounds, and other permissible oxygen valency angles. Table 8 summarises the calculations, and indicates that with a double " chair " conformation for dimethylenepentaerythritol, agreement between calculated and found values ${}_{m}K_2$) follows from variation of the oxygen valency angle rather than alteration of C–O bond polarisabilities.

[36] Otto, *J. Amer. Chem. Soc.*, 1937, **59**, 1590.

TABLE 8. *Dependence of* ${}_{\infty}({}_{m}K_2)$ *upon* C–O–C *valency angle and* C–O *bond polarisabilities.*

Oxygen angle	$10^{23}b_L^{C-O}$	$10^{23}b_T^{C-O}$	$10^{12}{}_{m}K$ (calc.)	Oxygen angle	$10^{23}b_L^{C-O}$	$10^{23}b_T^{C-O}$	$10^{12}{}_{m}K$ (calc.)
111°	0·081	0·039	−10·1 [a]	115° 20′	0·081	0·039	−11·1 [a]
,,	0·087	0·042	−10·9 [b]	,,	0·087	0·042	−11·9 [b]
,,	0·091	0·044	−11·4 [c]	,,	0·091	0·044	−12·5 [c]
113°	0·081	0·039	−10·9 [a]	117° 8′	0·081	0·039	−13·5 [a, d]
,,	0·087	0·042	−11·6 [b]	,,	0·087	0·042	−14·4 [b, d]
,,	0·091	0·044	−12·2 [b]	,,	0·091	0·044	−15·1 [c, d]

[a] C–O polarisabilities from paraldehyde.[3] [b] C–O polarisabilities from dioxan (unpublished). C–O polarisabilities from $R_{\infty}^{C-O} = 1{\cdot}500$ c.c. obtained by extrapolating the link refractivity listed by Vogel *et al.*[37] [d] In these three calculations the C–O distance taken was 1·41 Å in place of 1·43 Å.

For the " chair-boat " configuration semi-axes are:

$$b_1^{DMP} = b_2 + b_3{}^1 - 4b^{CH}$$
$$b_2^{DMP} = b_1 + b_1{}^1 - 4b^{CH}$$
$$b_3^{DMP} = b_3 + b_2{}^1 - 4b^{CH}$$

so that:

$$(2b_1 - b_2 - b_3)^{DMP} = 1{\cdot}20(b_L^{C-O} - b_T^{C-O})$$

and $\theta_2 = (1/45k^2T^2)[(2\mu_1{}^2 - \mu_2{}^2 - \mu_3{}^2)(b_L^{C-O} - b_T^{C-O})1{\cdot}20]$

where $\mu_1 = \mu_{res}\cos 47° 37'$, $\mu_2 = \mu_{res}\cos 34° 14'$ and $\mu_3 = \mu_{res}\cos 46° 45'$,

whence $\theta_2 = 0{\cdot}302$ and $\theta_1 = 0{\cdot}013$ (both $\times 10^{-35}$), and

${}_{m}K = 1{\cdot}3_2 \times 10^{-12}$

Summarising, we have for dimethylenepentaerythritol the value of $10^{12}{}_{m}K$ calculated for a double " chair " −10 to −15, and for a " chair–boat " + 1·3, the observed value being −19·6, from which the " double-chair " form is obviously to be preferred.

The award of a research scholarship (to M. R. S.) by the Australian Atomic Energy Commission is gratefully acknowledged.

UNIVERSITY OF SYDNEY, N.S.W., AUSTRALIA. [*Received, April 24th,* 1957.]

[37] Vogel, Cresswell, Jeffery, and Leicester, *J.*, 1952, 514.

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5. 2 : 3-5 : 6-8 : 9-*Tribenzoperinaphthene.*

By E. CLAR and D. G. STEWART.

1 : 2-Benzanthr-9-one gave the 10-benzylidene derivative (III), ring closure of which with aluminium chloride led to the hexacyclic ketone (IV). The reduction of this yielded the tribenzoperinaphthene (V) which was oxidised in the presence of acids to salts of type (VII).

THE skeleton of perinaphthene tends to form an aromatic framework with external, alternating single and double bonds and an odd electron or a positive charge in the centre (cf. I) Evidence for this assumption has accumulated recently.[1] We have now synthesised tribenzoperinaphthene derivatives and found that the same tendency occurs in this centrosymmetrical system.

1 : 2-Benzanthr-9-one (II) condensed smoothly with benzaldehyde in pyridine under the influence of piperidine, to form the derivative (III). Ring closure was then carried out with aluminium chloride in boiling benzene and is assumed to have yielded the hexacyclic ketone (IV), involving the more reactive naphthalene complex rather than the benzene complex. A by-product containing four hydrogen atoms more was also obtained, which could have a different skeleton since it could not be dehydrogenated to the ketone (IV). 2 : 3-5 : 6-8 : 9-Tribenzoperinaphthenone (IV) has basic properties: it forms a

[1] Boekelheide and Larrabee, *J. Amer. Chem. Soc.*, 1950, **72**, 1240, 1245; Clar, " Aromatische Kohlenwasserstoffe," Springer-Verlag, 1952, p. 431; Beckmann and Silberman, *Chem. and Ind.*, 1955, 1635; Sogo, Nokazaki, and Calvin, *J. Chem. Phys.*, 1957, **26**, 1343.

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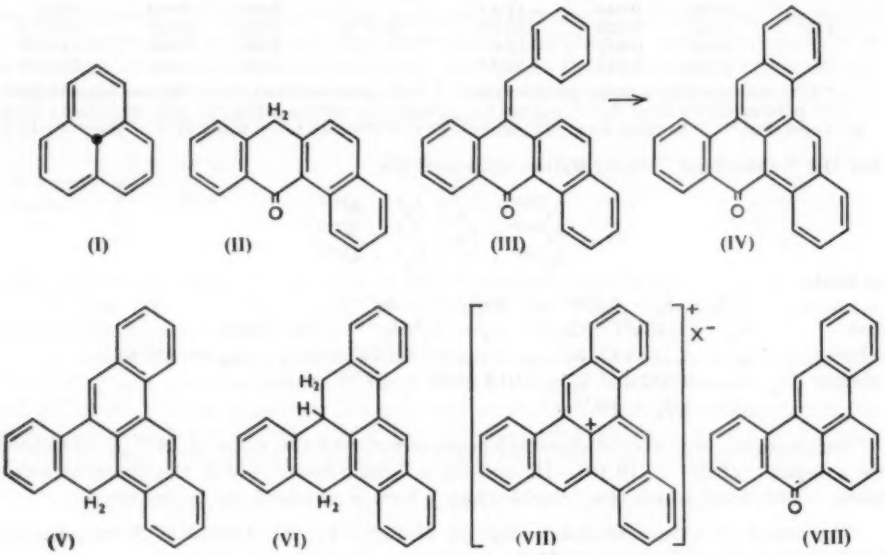
stable perchlorate. Reduction with hydriodic acid and red phosphorus gave, depending on the time of reaction, either 2 : 3-5 : 6-8 : 9-tribenzoperinaphthene (V) or its dihydro-derivative (probably VI). Whilst the tribenzoperinaphthene is fairly stable in neutral



solvents, it is quickly oxidised in acid by atmospheric oxygen. The solution in acetic acid became deep violet-blue when boiled in the presence of air or when selenium dioxide was added. The violet-blue solution was not stable, but was further oxidised to the

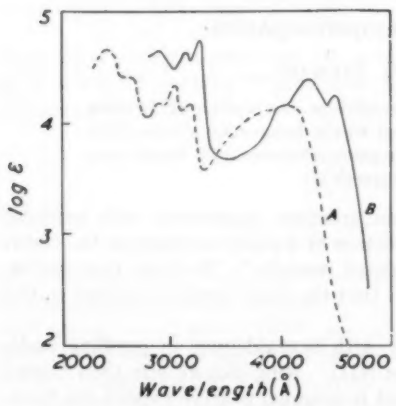


FIG. 1. *Absorption max.* (Å) *and* log ε (*in parentheses*).
A, 2 : 3-5 : 6-*Dibenzoperinaphthenone in* EtOH: 4040 (4·16); 3180 (4·15), 3030 (4·34), 2900 (4·18); 2410 (4·66).
B, 2 : 3-5 : 6-8 : 9-*Tribenzoperinaphthenone in* C_6H_6: 4520 (4·24), 4260 (4·40); 3260 (4·74), 3120 (4·64); 2860 (4·65).

tribenzoperinaphthenone (IV). However, it was stabilised by hydrochloric or perchloric acid. The crystalline, deep violet-blue perchlorate was not paramagnetic when tested with the microwave resonance absorption method.* This does not support a formula with an odd electron and proton in the centre of the molecule, and formula (VII) which

* This investigation was kindly carried out by Professor J. Weiss and Dr. P. A. Forrester, King's College, Newcastle.

has no radical character apparently accounts best for the properties of the tribenzoperinaphthylium perchlorate. The perchlorate gave a violet-blue solution in nitromethane; when alkali or pyridine was added the colour disappeared immediately, but if perchloric acid was then also added without delay the colour was restored. This also supports formula (VII) rather than the structure of a protonated radical.

The absorption spectra are in accordance with the structures here assumed. The long-wave absorption of the tribenzoperinaphthenone (IV) is much shifted towards the red in comparison with that of 2 : 3-5 : 6-dibenzoperinaphthenone [2] (VIII) (Fig. 1); this is to be expected owing to the annellation effect of a benzene ring fused linearly to the phenanthrene complex in (VIII) and extended to a 1 : 2-benzanthracene complex in

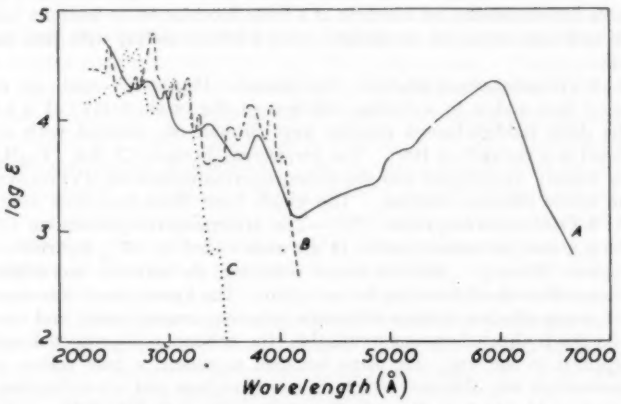


FIG. 2. *Absorption max.* (Å) *and* log ε (*in parentheses*).

A, 2 : 3-5 : 6-8 : 9-*Tribenzoperinaphthylium chloride in* 17% HCl: 5960 (4·36); 3820 (3·88), 3600 (3·70); 3350 (3·98); 2960 (4·26), 2780 (4·37).
B, 2 : 3-5 : 6-8 : 9-*Tribenzoperinaphthene in* EtOH: 4020 (3·68), 3930 (4·14), 3730 (4·16), 3540 (3·95); 3260 (4·04); 3160 (4·39), 3040 (4·33); 2840 (4·79), 2740 (4·50); 2460 (4·66).
C, *Dihydro*-2 : 3-5 : 6-8 : 9-*tribenzoperinaphthene in* EtOH: 3420 (2·87); 3160 (4·34), 3050 (4·37); 2690 (4·65), 2610 (4·64).

(IV). Also expected is the violet shift when the tribenzoperinaphthene (V) is compared with its dihydro-derivative (VI). The chloride (VII) (X = Cl), however, has an entirely different type of absorption (Fig. 2).

EXPERIMENTAL

M. p.s were taken in evacuated capillaries. Microanalyses are by Mr. Cameron and Miss M. W. Christie.

10-*Benzylidene*-1 : 2-*benzanthrone* (III).—1 : 2-Benzanthrone [3] (II) (48 g.), benzaldehyde (25 g.), pyridine (125 c.c.), and piperidine (1·25 c.c.) were boiled together for 4 hr. The solvent was then distilled off and the residue dried at 140° in a vacuum till free from benzaldehyde. The glassy product was dissolved in benzene and thoroughly extracted with warm alkaline sodium dithionite solution, till the red vat of the quinone was no longer formed. After being washed and dried, the benzene was removed and crystallisation from acetic acid gave yellow prisms (50 g.), m. p. 144—145°, of 10-*benzylidene*-1 : 2-*benzanthrone* (III) (Found: C, 90·1; H, 5·1. $C_{25}H_{16}O$ requires C, 90·3; H, 4·85%) which gave a magenta solution (no fluorescence) in concentrated sulphuric acid.

2 : 3-5 : 6-8 : 9-*Tribenzoperinaphthenone* (IV).—Powdered aluminium chloride (50 g.) was added to a solution of the ketone (III) (10 g.) in benzene (150 c.c.), and the deep red solution refluxed for 30 min. After decomposition the benzene layer was separated, washed, and dried.

[2] Clar, *Ber.*, 1943, **76**, 609.
[3] Cook, *J.*, 1930, 1087.

Chromatography on alumina with benzene as eluant gave first a colourless, non-fluorescent solution; concentration and crystallisation from xylene yielded colourless prisms (3 g.), m. p. 276—278° (Found: C, 89·7; H, 5·7. $C_{25}H_{16}O$ requires C, 89·75; H, 5·4%). The *compound* sublimed without decomposition in a vacuum, forming needles, m. p. 276—278°; it did not yield an acetate with acetic anhydride and gave a bright yellow, green-fluorescent solution in concentrated sulphuric acid. It was insoluble in alkaline solution and did not form a perchlorate. Attempts to dehydrogenate it with chloranil or palladium–charcoal and to oxidise it with selenium dioxide or chromic acid were unsuccessful. The second, yellow band in the chromatogram gave a clear yellow eluate whence concentration and crystallisation from acetic acid or benzene yielded orange-yellow needles (4 g.), m. p. 260—261°, of the *tribenzoperinaphthenone* (IV) (Found: C, 91·0; H, 4·3. $C_{25}H_{14}O$ requires C, 90·9; H, 4·3%) which gave a violet-red solution, with an orange fluorescence, in concentrated sulphuric acid. The compound, which gave stable brown needles on addition of a little bromine to its benzene solution, was not readily reduced and was recovered unchanged after 1 hour's boiling with zinc dust in pyridine and acetic acid.

2 : 3-5 : 6-8 : 9-*Tribenzoperinaphthenone Perchlorate.*—Perchloric acid (1 c.c.) in acetic anhydride (2 c.c.) was added to a boiling solution of the product (IV) (1 g.) in acetic acid. When cold, the dark reddish-brown needles were filtered off, washed with acetic acid and benzene, and dried in a vacuum at 100°. The *perchlorate* (Found: Cl, 8·4. $C_{25}H_{15}O_5Cl$ requires Cl, 8·25%) was readily hydrolysed and the tribenzoperinaphthenone (IV) recovered from it by means of warm dilute alkaline solution. The yields from these reactions were theoretical.

2 : 3-5 : 6-8 : 9-*Tribenzoperinaphthene* (V).—The tribenzoperinaphthenone (IV) (1 g.), red phosphorus (2·5 g.), and potassium iodide (1 g.) were added to 55% hydriodic acid (25 c.c.) covered with xylene (25 c.c.). After 48 hours' refluxing, the mixture was diluted with water, and the phosphorus filtered off from the hot solution. The xylene layer was separated, washed thoroughly with warm alkaline sodium dithionite solution, concentrated, and chromatographed on alumina. As the hydrocarbon was oxidisable, the column was protected against light and pressure was applied to the top. By using benzene as eluant, a pale yellow solution with a bright blue fluorescence was obtained which on concentration and crystallisation from benzene or methyl alcohol yielded pale yellow needles (0·6 g.), m. p. 253—255°, of the *tribenzoperinaphthene* (V) (Found: C, 94·4; H, 5·2. $C_{25}H_{16}$ requires C, 94·9; H, 5·1%). The hydrocarbon did not dissolve readily in concentrated sulphuric acid, but, on gentle warming, a violet-blue solution with a red fluorescence was obtained. A solution having the same colour was obtained by boiling the hydrocarbon in acetic acid in contact with air.

The hydrocarbon (0·2 g.) was dissolved in acetic acid (30 c.c.) containing perchloric acid (1 c.c.). A stream of oxygen was passed through the boiling solution, which rapidly assumed a deep violet-blue colour. After 15 min. the solution was allowed to cool and violet-blue crystals of the *perchlorate* were obtained, which were filtered off, washed with dry benzene, and dried in a vacuum (KOH) (Found: C, 71·5; H, 3·9. $C_{25}H_{15}O_4Cl$ requires C, 72·4; H, 3·6%). The blue solid was quickly decomposed by water to a yellow compound. The perchlorate was soluble in nitromethane, giving a violet-blue solution (red fluorescence), which became pale yellow on the addition of alkali or basic solvents such as pyridine. The initial colour of the solution was restored, however, by the addition of perchloric acid. The addition of perchloric acid to the solution after 15—30 min. gave the deep red colour of the perchlorate of tribenzoperinaphthenone (IV) and not that of the hydrocarbon perchlorate (V). The perchlorate in acetic acid was rapidly reduced by boiling it with zinc dust, and a colourless solution with a blue fluorescence was obtained which was re-oxidised on storage.

(? 3a : 4-)*Dihydro*-2 : 3-5 : 6-8 : 9-*tribenzoperinaphthene* (VI).—The tribenzoperinaphthenone (IV) (1 g.) was reduced for 5 days, under the conditions used for preparation of the tribenzoperinaphthene (V). The mixture was treated as described and the concentrated xylene layer was chromatographed on alumina with light petroleum (b. p. 40—60°) as eluant. A colourless non-fluorescent solution was obtained. Concentration and crystallisation from methyl alcohol gave yellow plates (0·5 g.), m. p. 178—180°, of the *dihydro-compound* (VI) (Found: C, 94·0; H, 5·7. $C_{25}H_{18}$ requires C, 94·3; H, 5·7%). This hydrocarbon did not dissolve in cold concentrated sulphuric acid but, on heating, a violet-blue solution with a red fluorescence was obtained. Boiling it in acetic acid in contact with oxygen did not affect the compound, but addition of a little selenium dioxide gave a violet-blue solution.

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6. *The Acid-catalysed Reversion of* L-*Arabinose and of* D-*Mannose.**

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The reversion by acids of L-arabinose and of D-mannose has been investigated. L-Arabinose is converted in part into 3- and 4-isomers of *O*-β-L-arabopyranosyl-L-arabinose; and β-L-arabopyranosyl β-L-arabopyranoside was separated from the mixture of oligosaccharides produced. D-Mannose yields a complex mixture of disaccharides and oligosaccharides from which 6-*O*-α- and 6-*O*-β-D-mannopyranosyl-D-mannose and (?) 4-*O*-β-D-mannopyranosyl-D-mannose have been isolated. The significance of these results is discussed.

The rate of hydrolysis of polysaccharides in solutions of dilute mineral acid depends mainly on the concentration of the acid and the temperature. Conversion of the polysaccharide into monosaccharide is never complete as the reaction is reversible and even under the most favourable conditions small amounts of oligosaccharide remain. Under less favourable conditions, that is high concentration of sugars, considerable quantities of oligosaccharide are formed in solution. One of the methods used to determine polysaccharide structure is to hydrolyse the polymer to smaller fragments which are then detected and separated chromatographically. In some cases the yields of oligosaccharides are very small and there is some doubt whether the isolated material is really part of the original polymer or whether it results from resynthesis (reversion) from smaller fragments which have been produced during the hydrolysis. As our interests have been in the chemistry of arabinose-, mannose-, and xylose-containing polymers the effect of acid on each of these three sugars has been studied. The object was to find which oligosaccharides are produced in conditions chosen such that a relatively large quantity of each monosaccharide is converted into oligosaccharides.

When L-arabinose was set aside in acid solution the optical rotation changed and oligosaccharides were readily detected chromatographically. It was very difficult to separate these oligosaccharides owing to the similarity of their chromatographic behaviour. However, after repeated fractionation on charcoal and cellulose columns, three disaccharides were separated and characterised. The major product was 3-*O*-β-L-arabopyranosyl-L-arabinose (A) which was conclusively identified. 4-*O*-β-L-Arabopyranosyl-L-arabinose (B) and *O*-β-L-arabopyranosyl β-L-arabopyranoside (C) were also separated and provisionally identified.

Disaccharide (A) was recognised by the formation of phenylosazone which was identical with that prepared from an authentic specimen. This identity was confirmed when the disaccharide was methylated and hydrolysed and the fragments were identified as 2 : 3 : 4-tri- and 2 : 4-di-*O*-methyl-L-arabinose.

Disaccharide (B), a chromatographically pure syrup, did not give a crystalline phenylosazone. Methylation gave a syrup which gave analytical figures of a hexamethyldipentoside and on hydrolysis furnished only 2 : 3 : 4-tri- and 2 : 3-di-*O*-methyl-L-arabinose. These were identified chromatographically and by the formation of crystalline derivatives of the corresponding acids. This evidence limits the structure of the disaccharide to structure (B) and 5-*O*-β-L-arabopyranosyl-L-arabofuranose.[2] Calculations of molecular rotation from Hudson's rule [3] show that structure (B) is preferred.

Disaccharide (C) can be separated chromatographically from the oligosaccharide mixture. It was obtained more readily when the mixture was boiled with aqueous sodium hydroxide, and the cooled solution then de-ionised on ion-exchange columns. This

* A preliminary account of this work was given in TAPPI, 1956, **39**, 438.

[1] Jones, *J.*, 1953, 1672.
[2] Cf. Stephen, *J.*, 1957, 1919.
[3] Hudson, *J. Amer. Chem. Soc.*, 1909, **31**, 537.

procedure destroyed all reducing sugars, the acidic decomposition products were absorbed, and the non-reducing disaccharide was found in the effluent from the column. It was characterised as the crystalline octa-acetate, the optical rotation (+232°) of which indicated that the two monosaccharide residues each possessed pyranose rings and β-glycosidic linkages. Calculations of molecular rotation by Hudson's rule confirm this view. It is of interest that the analogous α-linked trehalose-type disaccharide has been isolated after the action of sulphuric acid on D-arabinose.[5] The mixture of oligosaccharides produced on reversion of L-arabinose was very complex and contained several other di- and tri-saccharides which were not identified. If therefore hydrolysis of an arabinose-containing polymer produces only one disaccharide it is very probable that this is not formed by reversion, particularly if it is a disaccharide other than disaccharide (A). On the other hand, isolation of disaccharide (A) after hydrolysis of a polysaccharide, unless it is the only arabinobiose produced, may mean that reversion and synthesis of disaccharides has occurred.

When mannose is kept in 6N-hydrochloric acid the optical rotation of the solution rapidly becomes more positive and di- and oligo-saccharides can be detected on the chromatogram. The picture changes with time, some sugars, probably furanoside derivatives, which are formed initially, disappear and eventually an equilibrium of mono-, di-, tri-, and oligo-saccharides results. This equilibrium mixture was neutralised on an ion-exchange resin and the sugars were fractionated chromatographically, first on charcoal and then on cellulose columns. Four disaccharides were isolated and three were identified. These were (A) 6-*O*-α-D-, (B) 6-*O*-β-D-, (C) 3-*O*-α-D-, and (D) 4-*O*-β-D-mannopyranosyl-D-mannose.

Disaccharide (A) was obtained crystalline. Methylation followed by hydrolysis gave 2 : 3 : 4 : 6-tetra- and 2 : 3 : 4-tri-*O*-methyl-D-mannose which were characterised as the *N*-phenylmannosylamine [6] and as the derived lactone respectively.[7] This evidence proves that the sugars are linked either through position 5 or 6 of the reducing mannose moiety. Periodate oxidation of disaccharide (A) by Hough and Perry's method [8] yielded no formaldehyde, confirming this conclusion. Lead tetra-acetate oxidation [9] (Perlin, personal communication) proved that the disaccharide was the 1 : 6-derivative. Its optical rotation [3] indicates that the two mannose residues are joined by an α-glycosidic linkage.

The disaccharide (B) was a syrup which on methylation followed by hydrolysis gave a mixture identical with that isolated after hydrolysis of methylated disaccharide (A). On reduction it gave a syrupy mannitol derivative, one mole of which consumed six moles of periodate with the concomitant formation of four moles of formic acid, and one mole of formaldehyde, proving that compound (B) was the 1 : 6-β-linked disaccharide. Its optical rotation was in good agreement with the optical rotation calculated by Hudson's method.[10]

Component (C), 3-*O*-α-D-mannopyranosyl-D-mannose, was a syrup which on reduction with potassium borohydride, furnished a syrupy mannitol derivative, characterised as the crystalline deca-acetate. This mannitol derivative will also be produced when the 1 : 4-α-linked mannobiose is reduced and acetylated. Methylation of the reducing disaccharide gave an octamethyl derivative which on acidic hydrolysis yielded 2 : 3 : 4 : 6-tetra-*O*-methyl-D-mannose, identified as described above, and crystalline 2 : 4 : 6-tri-*O*-methyl-D-mannose [11] identified by comparison with an authentic specimen. The optical

[4] Cf. Hough and Jones, *J.*, 1953, 344.
[5] Rice, *J. Amer. Chem. Soc.*, 1956, **78**, 6167.
[6] Irvine and McNicoll, *J.*, 1910, 1452.
[7] Haworth, Hirst, and Streight, *J.*, 1931, 1349.
[8] Hough and Perry, *Chem. and Ind.*, 1956, 768.
[9] Charlson and Perlin, *Canad. J. Chem.*, 1956, **34**, 1805, 1811.
[10] Hudson, *J. Amer. Chem. Soc.*, 1916, **38**, 1566.
[11] Haworth, Heath, and Peat, *J.*, 1941, 833.

rotation indicated that the mannose residues are α-linked. These results were confirmed by Perlin[9] (personal communication) who subjected the disaccharide to oxidation with lead tetra-acetate and obtained yields of formic acid and consumption of oxidant in agreement with theory.

Disaccharide (D) was isolated in small amount, and was not obtained chromatographically pure as it moved at the same rate as disaccharide (A) on cellulose columns. However, when a crude sample of compound (D) was methylated and hydrolysed, in addition to 2 : 3 : 4 : 6-tetra-*O*-methyl-D-mannose, 2 : 3 : 4- and 2 : 3 : 6-tri-*O*-mannose were produced and detected chromatographically. Separation of the trimethyl fragments could be effected after the sugars had been converted by oxidation into the corresponding lactones. The identification of fraction (D) as a disaccharide rests on its rate of movement on the chromatogram.

The predominant sugar produced in this reversion was disaccharide (A), in which mannose residues are united through a primary alcohol group. This is to be expected because of the greater reactivity of that group. In addition, evidence was obtained of the presence of both a mannobiose of the trehalose type and a 1 : 6-mannosan. The experiment indicates that isolation of 1 : 6-linked mannose derivatives from a hydrolysate may result from reversion, but that if these are absent any other mannose disaccharides isolated are probably part of the structure of the polysaccharide which is undergoing hydrolysis. In this connection it will be noted that acidic hydrolysis of yeast mannan yielded 6-*O*-α-D-mannopyranosyl-D-mannose along with several other disaccharides. Acetolysis of yeast mannan [12] produced a different chromatographic picture, perhaps because the glycosidic linkage which is attached to a primary sugar-alcohol group is split more easily than those which are attached to secondary alcoholic groups. The two methods of hydrolysis may therefore be complementary. This isolation of the 1 : 6-linked mannobiose from yeast mannan cannot be taken as proving that 1 : 6-α-linked mannose residues are present in this polysaccharide.

It is concluded from this work and the accompanying paper that, in order to minimise the formation of acid reversion products, the hydrolysis of a polysaccharide shall be carried out in dilute solution, $\geqslant 5\%$ and preferably 2%. Great care should be taken to see that the sugar solution is neutral before it is concentrated and that no acidity has developed during the concentration. The isolation of an oligosaccharide which contains 1 : 6-linkages should not be regarded as proof of its presence in a particular polysaccharide unless it is isolated in large yield. It is suggested that the true products of hydrolysis of the polymer may be determined by conducting the hydrolysis in the presence of radioactive monomers. All oligosaccharides from the polymer will then be non-radioactive.

Experimental

Solutions were concentrated under reduced pressure at 40° or lower. Chromatographic separations were conducted on charcoal columns,[13] cellulose columns,[14] and paper sheets. The charcoal columns were a mixture (1 : 1 w/w) of activated carbon (Darco G-60) and "Celite" and were packed as a slurry in water. The cellulose columns were packed as a slurry of Whatman cellulose powder in acetone which was immediately replaced by the solvent to be used in the separation. Paper separations were conducted on sheets of Whatman No. 1 and 3MM chromatographic paper. Optical rotations were determined on aqueous solutions and at 20° ± 2° unless otherwise stated.

Charcoal columns were irrigated with water and/or ethanol. Various irrigants were used for paper chromatography: (*a*) ethyl acetate–acetic acid–water (9 : 2 : 2); (*b*) butan-1-ol–pyridine–water (10 : 3 : 3); (*c*) butan-1-ol–ethanol–water (40 : 11 : 19), (c_1) (3 : 1 : 1); (*d*) benzene–ethanol–water (169 : 47 : 15); (*e*) ethyl methyl ketone–water (89 : 11) [15] (all v/v). In general

[12] Smith and Srivastava, *J. Amer. Chem. Soc.*, 1956, **78**, 1404.
[13] Whistler and Durso, *ibid.*, 1950, **72**, 677.
[14] Hough, Jones, and Wadman, *J.*, 1949, 2511.
[15] Partridge, *Biochem. J.*, 1948, **42**, 238.

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solvent (*a*) was used to separate monosaccharides and certain of their derivatives, (*b*), (*c*), and (c_1) were used to separate disaccharides, and (*d*) and (*e*) to separate partially methylated monosaccharides. The eluates from cellulose columns were collected on an automatic fraction-collector.[14]

Sugars were detected on paper chromatograms by spraying with a 1% solution of *p*-anisidine hydrochloride [16] in butan-1-ol and heating (for reducing sugars) or with a 1% solution of silver nitrate in acetone followed by spraying with 2% ethanolic sodium hydroxide for non-reducing sugars.[17] Lactones were detected by the hydroxamic acid test.[18] The rates of movement of of sugars are quoted relative to a standard sugar, *e.g.*, R_{gal}, R_{Rh}, and R_G (relative to galactose, rhamnose, and 2 : 3 : 4 : 6-tetra-*O*-methyl-D-glucose respectively).

Reversion of L-*Arabinose.*—L-Arabinose (76 g.) which contained a small amount of galactose (chromatographic evidence) was dissolved in 6N-hydrochloric acid (400 ml.), and the solution set aside for 96 hr. during which the change in optical rotation was followed: $[\alpha]_D$ +51·5° (0·75 hr.); 52·3° (2 hr.); 53·4° (4 hr.); 55·5° (8 hr.); 61·2° (24 hr.); 68·3° (48 hr.); 72·0° (96 hr.). The solution was then diluted and deacidified on Amberlite resin IR-4B(OH), and the neutral effluent was concentrated to a syrup. The syrupy product was then separated on a charcoal–Celite column [13] by passing water (fraction I), and then 5% ethanol–water (fraction II, III, and IV) through the column. The results are given in Table 1.

TABLE 1

Fraction	R_{gal} (irrigant *a*)	Wt. (g.)	Fraction	R_{gal} (irrigant *a*)	Wt. (g.)
I	Arabinose	33·7	III	1·2, 0·8, 0·5, 0·4, 0·2	5·2
II	Arabinose, 0·8, 0·4	25·6	IV	0·75, 0·5, 0·3	7·4
					71·9

Fraction II crystallised and the crystals were identified as L-arabinose; the residual syrup (13·2 g.) was almost free from L-arabinose. It was further fractionated on a cellulose column,[14] with butan-1-ol–water (10 : 1 v/v) as irrigant. When solvent (*b*) was used to examine the fraction obtained it was observed that the mixture was much more complex than was indicated by solvent system (*a*). Solvent (*b*) indicated the presence of components with R_{gal} 1·2, 0·72, 0·61, 0·55, 0·43, 0·36, 0·33, 0·28, and 0·23. In a similar fashion fractions III and IV were shown to be complex mixtures, and additional fractions were detected with R_{gal} 0·40 and 1·04.

After tedious further fractionation, first on cellulose columns and then on sheets of filter paper, a fraction (0·22 g.) with R_{gal} 0·76 (solvent *b*) was obtained chromatographically pure. It had $[\alpha]_D^{23}$ 192° (*c* 4·3) and when heated with phenylhydrazine acetate solution gave an osazone, m. p. 234°. This material was identical with the osazone of 3-*O*-β-L-arabopyranosyl-L-arabinose. A pure fraction with R_{gal} 0·55 (solvent *b*) was also isolated after a protracted series of fractionations. This substance (0·46 g.) had $[\alpha]_D$ 193° (*c* 5·0) and did not crystallise. A sample (0·35 g.) was methylated, first with sodium hydroxide and dimethyl sulphate and then with silver oxide and methyl iodide. The *product* had n_D^{21} 1·4710, b. p. 180° (bath-temp.)/0·05 mm., and $[\alpha]_D$ 128° (*c* 3·6 in $CHCl_3$) (Found: C, 52·7; H, 8·0; OMe, 49·2. $C_{16}H_{30}O_9$ requires C, 52·4; H, 8·3; OMe, 50·6%).

The syrupy material was hydrolysed by N-sulphuric acid at 93° for 4 hr. and neutralised with barium carbonate. The solution was filtered and concentrated to a syrup (0·29 g.) with $[\alpha]_D$ 136° (*c* 2·5), 64° (*c* 2·43 in $CHCl_3$). The material consisted of two sugars with R_{gal} 0·69 and 0·84 (solvent *b*) and R_{gal} 0·52 and 0·84 (solvent *d*). The mixture was separated on a sheet of filter paper (solvent *b*). The slower-moving fraction (0·06 g.) had $[\alpha]_D$ 92° (*c* 2·8) and was identical, chromatographically, with 2 : 3-di-*O*-methyl-L-arabinose. On oxidation by bromine water it yielded the well-characterised 2 : 3-di-*O*-methyl-L-arabonolactone, m. p. 35°, $[\alpha]_D$ −36° ⟶ −28° (10 days) (*c* 1·1). The faster-moving fraction (0·99 g.) had $[\alpha]_D$ 125° (*c* 4·7) and on oxidation with bromine water gave a lactone which when heated with alcoholic phenylhydrazine yielded 2 : 3 : 4-tri-*O*-methyl-L-arabonyl phenylhydrazide, m. p. 158°, identical with an authentic specimen.

When the disaccharide described above was acetylated there was obtained in very small yield an unidentified crystalline acetate, m. p. 167°.

[16] Hough, Jones, and Wadman, *J.*, 1950, 1702.
[17] Trevelyan, Procter, and Harrison, *Nature*, 1950, **166**, 444.
[18] Abdel-Akher and Smith, *J. Amer. Chem. Soc.*, 1951, **73**, 5859.

Isolation of O-β-L-*Arabopyranosyl* β-L-*Arabopyranoside.*—L-Arabinose (16 g.) was dissolved in 6N-hydrochloric acid (20 ml.) and set aside at room temperature for 96 hr. Excess (25 ml.) of 10N-sodium hydroxide was added and the mixture was boiled under reflux for 5 hr. The cooled solution was de-ionised by Amberlite resins IR-120(H) and IR-4B(OH), and concentrated to a syrup (1·31 g.). The syrup was acetylated with pyridine (20 ml.) and acetic anhydride (8 ml.) for 48 hr. at room temperature and then poured into ice-water. The acetate was isolated by chloroform-extraction and slowly crystallised. The crystals, recrystallised from alcohol (yield, 0·02 g.), had m. p. 232°, $[\alpha]_D$ 232° (*c* 0·15 in $CHCl_3$) (Found: C, 49·6; H, 5·7. Calc. for $C_{22}H_{36}O_{15}$: C, 49·5; H, 5·6%).

Reversion of D-*Mannose.*—D-Mannose (75 g.) was dissolved in 6N-hydrochloric acid (125 ml.) and the solution was kept at room temperature for 168 hr., during which the change in optical rotation was: $[\alpha]_D$ +6·67° (initial); +7·09° (1 hr.); +8·77° (8 hr.); +9·46° (24 hr.); +9·88° (36 hr.). The solution was then diluted and deacidified by passing it down a column of Amberlite IR-4B(OH) resin. The neutral effluent was concentrated to a syrup and placed on a charcoal column (15 × 17 cm. diam.) and eluted with water (portions of 125 ml.). In this fashion seven fractions were obtained (see Table 2). When fractions 3 and 6 were refractionated on columns of cellulose the component with R_{gal} 0·39 (solvent c_1), *disaccharide* A, was obtained pure and crystalline. After recrystallisation from methanol–butan-1-ol it had m. p. 196—197°, $[\alpha]_D^{16}$ +52° (*c* 1·99) (Found: C, 42·2; H, 6·4. $C_{12}H_{22}O_{11}$ requires C, 42·1; H, 6·4%).

TABLE 2.

Fraction	R_{gal} (solvent c_1)	Wt. (g.)	Fraction	R_{gal} (solvent c_1)	Wt. (g.)
1	mannose	20·7	5	mannose, 0·54, 0·49, 0·39	0·7
2	mannose, 0·54, 0·39	19·9	6	0·54, 0·49, 0·49 high mol. wt.	10·7
3	2·6, 0·54, 0·39	10·3	7	0·54, high mol. wt.	10·9
4	0·39	1·9			
					75·1

Methylation of the Disaccharide A.—A portion (0·82 g.) of the crystalline reducing disaccharide was methylated with sodium hydroxide and methyl sulphate in the usual way. The *product* (0·58 g.), n_D^{18} 1·4640, distilled at b. p. 192° (bath-temp.)/0·1 mm. The distillate (0·40 g.) had $[\alpha]_D$ +58° (*c* 3·74 in $CHCl_3$) (Found: C, 52·8; H, 8·3; OMe, 54·4. $C_{20}H_{38}O_{11}$ requires C, 52·9; H, 8·4; OMe, 54·6%). The methylated product (0·34 g.) was hydrolysed in N-sulphuric acid (15 ml.) at 100° for 162 hr., during which the optical rotation changed from +40° to +6°. The solution was neutralised with barium carbonate and concentrated to a syrup (0·3 g.) which was fractionated on sheets of Whatman No. 3MM filter paper. The slower-moving component, with R_F 0·55 (0·09 g.), had $[\alpha]_D$ +3° (*c* 0·37) (Found: OMe, 41·8. Calc. for $C_9H_{18}O_6$: OMe, 41·9%.) It was oxidised with bromine water and yielded 2 : 3 : 4-tri-*O*-methyl-D-mannonolactone, which moved at the same rate on the chromatogram as an authentic specimen (R_F 0·75, solvent c_1, hydroxamic acid spray) and had m. p. and mixed m. p. 72—73°, $[\alpha]_D$ 136° ⟶ +82° (85 hr.) (*c* 0·28). The faster-moving component (0·12 g.), with R_F 0·78 (solvent *e*), had $[\alpha]_D$ 2·9° (*c* 0·45). When this syrup was heated with alcoholic aniline the *N*-phenylglycosylamine 2 : 3 : 4 : 6-tetra-*O*-methyl-D-mannose resulted, with m. p. 164—165° which fell to 144—145° after recrystallisation from ethanol, $[\alpha]_D$ 95° ⟶ −7° (137 hr.; *c* 0·59 in MeOH) (Found: C, 61·6; H, 8·1; N, 4·7. Calc. for $C_{16}H_{25}O_5N$: C, 61·7; H, 8·0; N, 4·5%).

The component in fraction 3, with R_{gal} 2·6 (solvent c_1), was non-reducing and was detected with the silver nitrate spray. It was present in small amount and had $[\alpha]_D$ −79° (*c* 0·29). It was not identified but may be 1 : 6-anhydro-β-*O*-D-mannopyranose.

The disaccharide with R_{gal} 0·54 (solvent c_1), disaccharide C, was obtained pure by refractionation, on a cellulose column, of fraction 3. The substance (1·43 g.) had $[\alpha]_D$ +50° (*c* 2·86).

Methylation of Disaccharide C.—A portion of the reducing disaccharide (0·72 g.) was methylated in the usual way with methyl sulphate and sodium hydroxide and then with silver oxide and methyl iodide. The product (0·7 g.) distilled at 197° (bath-temp.)/0·3 mm. as a syrup (0·48 g.) (Found: C, 53·0; H, 8·3; OMe, 54·8. $C_{20}H_{38}O_{11}$ requires C, 52·9; H, 8·4; OMe, 54·6%). The methylated *product* (0·47 g.) was hydrolysed with 45% formic acid (25 ml.) at 100° for 7 hr., $[\alpha]_D$ 64° falling to 19° (const.). The solution was evaporated to a syrup which was heated for 1 hr. with N-sulphuric acid, in order to hydrolyse formyl esters. The solution was then extracted continuously with chloroform and the extracts were concentrated to a syrup (0·46 g.). The mixture was separated chromatographically (solvent *e*). The slower-moving of the components (0·15 g.) crystallised and after recrystallisation from acetone–light

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petroleum had m. p. 64—65°, unchanged on admixture with 2 : 4 : 6-tri-*O*-methyl-D-mannose, and $[\alpha]_D$ + 16·5° (*c* 3·0). The faster-moving component (0·17 g.) had $[\alpha]_D$ +3° (*c* 1·7) and with ethanolic aniline gave the *N*-phenylglycosylamine, m. p. 144°, of 2 : 3 : 4 : 6-tetra-*O*-methyl-D-mannose.

Reduction.—A portion of the reducing disaccharide (0·20 g.) was dissolved in water and reduced by the portionwise addition of an excess of potassium borohydride. The solution was acidified with acetic acid and de-ionised on Amberlite resin IR-120 and IR-4B. The neutral solution was evaporated to the syrupy mannitol derivative (0·17 g.), R_{Ga} 0·37 (solvent *a*), $[\alpha]_D$ +59° (*c* 1·7 in MeOH). The syrup was acetylated in pyridine (5 ml.) and acetic anhydride (2 ml.) at 20° for 30 hr. The *product* (0·35 g.) had m. p. 116° (from ethanol), $[\alpha]_D$ 47° (*c* 2·2 in acetone) (Found: C, 50·1; H, 5·7. $C_{30}H_{42}O_{20}$ requires C, 49·9; H, 5·8%).

Fraction 6 was further fractionated on several sheets of Whatman No. 3MM paper and gave two chromatographically pure disaccharides (R_{gal} 0·39 and 0·51). The disaccharide fraction B, with R_{gal} 0·39 (0·5 g.), had $[\alpha]_D$ +12·4° (*c* 1·8), and gave on hydrolysis only D-mannose. A portion (0·1 g.), on reduction of its aqueous solution with potassium borohydride, gave the syrupy mannitol derivative (0·098 g.), $[\alpha]_D$ −21° (*c* 1·0).

The mannitol derivative (0·098 g.) was oxidised with 0·06M-sodium metaperiodate (100 ml.), and the solution was analysed at intervals for formic acid produced and metaperiodate consumed. After 4 hr. four moles of formic acid had been produced and 6 moles of periodate reduced per mole.

Methylation of Disaccharide B.—The reducing disaccharide (0·25 g.) was methylated, first with sodium hydroxide and methyl sulphate and then with silver oxide and methyl iodide. The pure *product* (0·21 g.) had n_D^{21} 1·4621, $[\alpha]_D$ −26° (*c* 2·1 in $CHCl_3$) (Found: OMe, 54·7. $C_{20}H_{36}O_{11}$ requires OMe, 54·6%). It was hydrolysed by heating its solution in N-sulphuric acid (25 ml.) at 98° for 7 hr., $[\alpha]_D$ −19° ⟶ +3°. When hydrolysis was complete the solution was extracted continuously with chloroform and the extracts were concentrated to a syrup (0·19 g.). The methylated components were separated (solvent *d*) by filter-paper chromatography. The tri-*O*-methyl fraction (0·05 g.) had $[\alpha]_D$ 1·6° (*c* 2·5). Oxidation with bromine water converted it into 2 : 3 : 4-tri-*O*-methyl-D-mannonolactone, m. p. and mixed m. p. 72—73°, $[\alpha]_D^{23}$ 130° ⟶ 81° (90 hr.). The tetra-*O*-methyl-D-mannose fraction (0·08 g.) was characterised as 2 : 3 : 4 : 6-tetra-*O*-methyl-*N*-phenyl-D-mannosylamine, m. p. 145°.

Methylation of Disaccharide D.—The substance with R_{gal} 0·51 (solvent c_1) (0·2 g.), $[\alpha]_D$ −8·5° (*c* 2·0), was methylated with methyl sulphate and sodium hydroxide and then with silver oxide and methyl iodide. The methylated *product* (0·15 g.) had $[\alpha]_D$ −12° (*c* 3·1 in $CHCl_3$) and n_D^{20} 1·4640 (Found: OMe, 54·1. $C_{20}H_{36}O_{11}$ requires OMe, 54·6%). The methylated material was hydrolysed by N-sulphuric acid (15 ml.) at 95°, $[\alpha]_D$ −17° changing to +18° (7 hr.). The hydrolysis mixture was extracted continuously with chloroform, and the extracts were concentrated to a syrup (0·13 g.), which was separated on sheets of Whatman No. 1 filter paper. The tetra-*O*-methyl fraction (0·05 g.) was characterised as the crystalline *N*-phenylmannosylamine derivative, m. p. 145°. The tri-*O*-methyl fraction (0·09 g.) was a mixture which could not be separated chromatographically. Accordingly it was oxidised (bromine water) and the lactones were isolated. These crystallised in part. Paper-chromatographic separation of the mixture indicated (tentatively) the presence of the 2 : 3 : 6- and 2 : 3 : 4-tri-*O*-methyl isomers of D-mannonolactone (detected by the hydroxylamine spray).

Hydrolysis of Yeast Mannan.—Yeast mannan (2 g.) was hydrolysed in 0·5N-sulphuric acid (50 ml.) for 10 hr. at 100°. The hydrolysis mixture was neutralised with barium carbonate, filtered, and evaporated to a syrup (1·83 g.). Paper chromatography of its solution (solvent c_1) indicated the presence of mannose and four disaccharides with R_{gal} 0·58, 0·51, 0·42, and 0·36, the third disaccharide predominating. The syrup was fractionated on filter paper and the portions with R_{gal} 0·42 isolated. This material crystallised and was recrystallised from methanol–butan-1-ol. The substance (0·18 g.) had m. p. 196—197°, not depressed on admixture with 6-*O*-α-D-mannopyranosyl-D-mannose. It had $[\alpha]_D$ +53° (*c* 1·8) (Found: C, 42·1; H, 6·2. Calc. for $C_{12}H_{22}O_{11}$: C, 42·1; H, 6·4%). When D-mannose (1·8 g.) was heated in 0·5N-sulphuric acid (50 ml.) at 100° for 10 hr. it was converted in part into a mixture of oligosaccharides. The solution was neutralised as above, filtered, and concentrated. Chromatography of the syrup gave a picture very similar to that produced when hydrolysed yeast mannan was examined chromatographically.

Acetolysis of Yeast Mannan.[12]—Yeast mannan (2·3 g.) was added in small portions to a

well-stirred mixture of acetic anhydride (8·8 ml.) and sulphuric acid (0·9 ml.) at 0°. After 2 hr. at 0° the solution was stirred at 20° for 12 hr. Acetic anhydride (2·3 ml.) was then added and stirring continued for a further 33 hr. at 20° and then at 90° for 15 min. The cooled mixture was poured on ice, and the acetylated product collected. The white powder (2·4 g.) was deacetylated catalytically [19] and the product examined chromatographically. Mannose, a disaccharide, and a trisaccharide were detected. The disaccharide had R_{gal} 0·59 (solvent c_1); the disaccharide with R_{gal} 0·42 was present in traces only.

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[19] Zemplen, *Ber.*, 1926, **59**, 1254; 1927, **60**, 1555.

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7. *The Acid-catalysed Reversion of* D-*Xylose.*

By D. H. BALL and J. K. N. JONES.

Treatment of D-xylose with 6N-hydrochloric acid has yielded a mixture of oligosaccharides in addition to the starting material. Five disaccharides were isolated, three of them crystalline, namely, xylobiose, *O*-α-D-xylopyranosyl α-D-xylopyranoside, and 3-*O*-α-D-xylopyranosyl-D-xylose. The other two disaccharides were the 2- and the 4-*O*-isomer of the last-named sugar.

As in the case of L-arabinose (preceding paper), D-xylose is converted by 6N-hydrochloric acid into a mixture of xylose and xylose-containing oligosaccharides. The complex mixture was fractionated by chromatography on charcoal and cellulose columns. Three crystalline disaccharides were isolated and identified: (1) xylobiose, (2) *O*-α-D-xylopyranosyl α-D-xylopyranoside, and (3) 3-*O*-α-D-xylopyranosyl-D-xylose. In addition, evidence was obtained for the presence of (4) 4- and (5) 2-*O*-α-D-xylopyranosyl-D-xylose.

Xylobiose, which has been obtained previously on hydrolysis of xylan,[1] was characterised as the crystalline sugar and its phenylosazone.

Disaccharide (2) was a non-reducing sugar which could not be detected on paper chromatograms with the *p*-anisidine hydrochloride spray [2] but reduced the silver nitrate spray reagent of Trevelyan *et al.*[3] This sugar crystallised along with sugar (3), but was separated from it after the mixture had been reduced and then acetylated. Oxidation of sugar (2) with lead tetra-acetate (4 moles) yielded 2 moles of formic acid per mole of sugar, proving the presence of two unsubstituted xylopyranose residue in the disaccharide. The molecular rotation agreed well with that calculated for an α : α-linked xylobiose of the trehalose type by Hudson's rule.[4]

The crystalline disaccharide (3) was oxidised with the consumption of 3 mols. of lead tetra-acetate, and concomitant formation of 1 mol. of formic acid. No formaldehyde was produced. In the non-catalysed oxidation of the disaccharide, 1 mol. of oxidant was consumed rapidly within five minutes, and further oxidation was very slow.[5] Hydrolysis of the oxidised product gave equimolecular quantities of D-xylose and D-threose. Previous

[1] Whistler and Tu, *J. Amer. Chem. Soc.*, 1951, **73**, 1389; Whistler, Bachrach, and Tu, *ibid.*, 1952, **74**, 3059.
[2] Hough, Jones, and Wadman, *J.*, 1950, 1702.
[3] Trevelyan, Procter, and Harrison, *Nature*, 1950, **166**, 444.
[4] Hudson, *J. Amer. Chem. Soc.*, 1909, **31**, 66; 1916, **38**, 1566.
[5] Charlson and Perlin, *Canad. J. Chem.*, 1956, **34**, 1200.

experiments [6] have shown that these are the results expected from the oxidation of a 1 ⟶ 3-linked dipentoside. Calculations of molecular rotation [4] indicated that the two xylose residues are joined by an α-glycosidic linkage. Reduction of the sugar gave a xylitol derivative which, on oxidation with metaperiodate at pH 8, gave 2·5 mols. of formaldehyde. This result confirmed the presence of a 1 ⟶ 3 linkage in the disaccharide; 1 ⟶ 2, 1 ⟶ 4, and 1 ⟶ 5-linked disaccharides would liberate only 1 mol. of formaldehyde under these conditions, since they are not readily overoxidised.[7]

Identification of the fourth and the fifth sugar is not so conclusive, since they were obtained as an inseparable syrup. Methylation of the mixture of sugars gave a hexamethyl derivative which, on hydrolysis, yielded crystalline 2 : 3 : 4-tri- and 2 : 3-di-*O*-methyl-D-xylose. The syrup remaining after crystallisation of the 2 : 3-di-*O*-methyl-D-xylose was oxidised, and crystalline 3 : 4-di-*O*-methyl-D-xylonolactone [8] was obtained from the product. These results show that the xylose residues were probably linked through positions 4 and 2 respectively in the two disaccharides. Since the syrupy mixture of disaccharides was chromatographically distinct from xylobiose (4-*O*-β-D-xylopyranosyl-D-xylose), it was inferred that the 1 ⟶ 4-linked component contained an α-linkage. Further, the optical rotation of the syrup was such that both components probably contained α-glycosidic linkages, and that the xylose units were probably in the pyranose form. Experience has shown that xylofuranosides move faster on paper chromatograms than the corresponding pyranosides. Since these two sugars move more slowly on chromatograms than does the disaccharide (2), which is a xylopyranose derivative, it is inferred that they contain pyranose residues only.

These results indicate that the isolation of α-linked xylose-containing disaccharides on hydrolysis of a xylose-containing polymer should be treated with reserve. If more than one such disaccharide is detected in the hydrolysate, they may be reversion products. On the other hand, the formation of one disaccharide only is indication that it is not an artefact.

Experimental

Paper chromatography was carried out by the descending method [9] on Whatman No. 1 filter paper, the following solvent systems being used: (*a*) butanol-1-ol–ethanol–water (3 : 1 : 1), (*b*) butan-1-ol–pyridine–water (10 : 3 : 3), (*c*) ethyl acetate–acetic acid–water (9 : 2 : 2), and (*d*) ethyl acetate–acetic acid–formic acid–water (18 : 3 : 1 : 4) (all v/v). The positions of the sugars on the chromatograms were determined by spraying them either with silver nitrate in acetone followed by sodium hydroxide in ethanol [2] or with *p*-anisidine hydrochloride in butan-1-ol.[3] The rates of movement of the sugars are quoted relative to that of galactose (R_{gal}) or rhamnose (R_{rh}) on the same chromatogram. Optical rotations were determined on aqueous solutions at 23° ± 3° and are equilibrium values unless otherwise stated. Solvents were removed under reduced pressure.

Formation of Oligosaccharides.—To D-xylose (80 g.), dissolved in water (80 ml.), was added concentrated hydrochloric acid (80 ml.). After 6 days, no further change in the composition of the reversion mixture could be detected on paper chromatograms. The dark solution was filtered through " Celite " and stirred for 24 hr. with Amberlite resin IR-4B. The last traces of acid were removed by passing the solution down a column of this resin. Concentration of the neutral effluent afforded a syrup which consisted of xylose and a highly complex mixture of oligosaccharides (as detected by chromatography with solvents *a*, *b*, *c*, and *d*.)

Fractionation of the Oligosaccharides.—The syrup, dissolved in a little water, was applied to the top of a column of charcoal (Darco G60) and Celite (1 : 1; w/w) of 12·2 cm. diameter and of 13 cm. depth. The column was eluted with water and then with increasing concentrations of ethanol in water,[10] and the fractionation was followed paper-chromatographically.

[6] Perlin, *Analyt. Chem.*, 1955, **27**, 396.
[7] Hough and Perry, *Chem. and Ind.*, 1956, 768.
[8] James and Smith, *J.*, 1945, 739.
[9] Partridge, *Biochem. J.*, 1948, **42**, 238.
[10] Whistler and Durso, *J. Amer. Chem. Soc.*, 1950, **72**, 677.

The first fraction (A) (41·5 g.) consisted of D-xylose. The next four fractions (B, 1·0 g.; C, 10·8 g.; D, 0·9 g.; and E, 1·8 g.) contained oligosaccharides.

Fraction (C) contained sugars having R_F values in the range expected for pentose-containing disaccharides only. On paper chromatograms, developed in solvent *b*, and sprayed with the *p*-anisidine hydrochloride reagent, three major spots, α, β, and γ, were apparent, having R_{gal} values of 1·25, 1·2, and 0·75, respectively. Fraction C was therefore refractionated on cellulose columns, with butan-1-ol–water (15 : 1 v/v) as the mobile phase. In this way, three sub-fractions, C_1, C_2, and C_3 were obtained, which, on paper chromatograms sprayed with the *p*-anisidine hydrochloride reagent, gave single spots corresponding to α, β, and γ respectively.

Separation of Fraction C_1 into Reducing and Non-reducing Components.—When chromatograms of fraction C_1 were sprayed with the silver nitrate reagent, another spot was observed in addition to that detected by the *p*-anisidine hydrochloride reagent; it had R_{gal} 1·15 (solvent *b*). On storage, fraction C_1 crystallised in part, and it was divided into crystalline and non-crystalline portions (C_1' and C_1'' respectively). By means of paper chromatography, with both spray reagents, it was shown that the crystalline fraction C_1' was a reducing sugar, and that the syrup C_1'' was enriched with the non-reducing component.

In an attempt to obtain the non-reducing sugar in a pure condition, fraction C_1'' (0·36 g.) was acetylated with anhydrous sodium acetate (0·36 g.) and acetic anhydride (4·0 ml.) at 80—100° for 4 hr. The yellow mixture was poured into water, and the resulting crystalline acetates were recrystallised from methanol. The product had m. p. 180—240°, indicating that no fractionation of acetates had occurred. Further recrystallisation did not alter the m. p. (Found: C, 49·5; H, 5·8; OAc, 49·6. Calc. for $C_{22}H_{30}O_{15}$: C, 49·4; H, 5·7; OAc, 48·3%).

Fraction C_1'' (0·51 g.) was dissolved in water and reduced with sodium amalgam, the pH being kept at 7—9 by addition of acetic acid. The non-reducing solution was then freeze-dried, and the residue acetylated with pyridine and acetic anhydride. The resulting mixture of acetates crystallised in part; the crystalline portion, recrystallised from ethanol, had m. p. 242—250° and $[\alpha]_D$ +159° (*c* 1·25 in $CHCl_3$) (Found: C, 49·8; H, 5·7; OAc, 49·7. $C_{22}H_{30}O_{15}$ requires C, 49·4; H, 5·7; OAc, 48·3%).

This crystalline *acetate* was de-acetylated catalytically. A crystalline *sugar* was obtained which, after recrystallisation from moist methanol, had m. p. 269—272°, $[\alpha]_D$ +210° (*c* 1·0) (Found: C, 42·7; H, 6·4. $C_{10}H_{16}O_9$ requires C, 42·6: H, 6·4%). Hydrolysis of this material gave xylose only. Oxidation with lead tetra-acetate resulted in the uptake of 4 mols. of oxidant and the liberation of 2 moles of formic acid per mole of sugar, but no formaldehyde (chromotropic acid test).[11]

3-O-α-D-*Xylopyranosyl*-D-*xylose.*—After recrystallisation from methanol, fraction C_1' had m. p. 178° and $[\alpha]_D$ +106° (5 min.), +118° (75 min., const.; *c* 1·0). The compound moved as one spot on paper chromatograms and had R_{gal} 1·05 (solvent *a*) and 1·25 (solvent *b*).

The disaccharide was oxidised by lead tetra-acetate in 5 hr. with the consumption of 3 mols. of lead tetra-acetate and formation of 1 mol. of formic acid, but no formaldehyde. In the non-catalysed oxidation (no potassium acetate) of the disaccharide,[5] 1 mol. of oxidant was consumed in 5 min. and, after hydrolysis of the oxidised compound, xylose and threose were detected chromatographically.

The crystalline disaccharide (10 ml.) was reduced in water with potassium borohydride.[12] The solution was neutralised with acetic acid and de-ionised with Amberlite resins IR-120 and IR-4B. Concentration then gave a syrup (8 mg.) which moved as one spot on paper chromatograms (R_{gal} 1·0, solvent *a*). It was not detectable with the *p*-anisidine hydrochloride spray. A portion of the syrup was oxidised with periodate at pH 8 and the yield of formaldehyde was determined colorimetrically (chromotropic acid test): 1·29 (3 min.); 1·61 (8 min.); 2·24 (20 min.); 2·42 (50 min.); 2·53 (350 min.); 2·45 equivs. (500 min.).

Identification of Two Disaccharides in Fraction C_2 as 4- *and* 2-*O*-α-D-*Xylopyranosyl*-D-*xylose.*—Fraction C_2, a syrup, had $[\alpha]_D$ +77° (*c* 7·1) and did not yield a crystalline osazone. It behaved as a single compound on paper chromatograms. A portion (0·50 g.) was methylated with methyl sulphate and alkali in the usual way. The product (0·39 g.) had n_D^{20} 1·4627 and crystallised in part. The crystals were separated and, after recrystallisation from *n*-hexane,

[11] Boyd and Logan, *J. Biol. Chem.*, 1942, **146**, 279.
[12] Wolfrom and Wood, *J. Amer. Chem. Soc.*, 1951, **73**, 2933; Abdel-Akher, Hamilton, and Smith, *ibid.*, p. 4691.

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the *ether* had m. p. 109°, $[\alpha]_D$ +50° (*c* 1·86 in MeOH) (Found: C, 52·5; H, 8·1; OMe, 50·5. $C_{16}H_{30}O_9$ requires C, 52·5; H, 8·3; OMe, 50·8%).

A portion (85 mg.) of the ether was hydrolysed by N-sulphuric acid at 90° for 5 hr. and the component sugars were separated on sheets of filter paper (solvent *a*). The faster-moving sugar (30 mg.) was identified as 2 : 3 : 4-tri-*O*-methyl-D-xylose, m. p. and mixed m. p. 86—88°. The slower-moving compound (25 mg.) crystallised and had m. p. 82—85°, not depressed on admixture with 2 : 3-di-*O*-methyl-D-xylose, m. p. 86—88°. The identity was confirmed by *X*-ray powder photography.

The syrup remaining after the removal of the crystalline methylated disaccharide had $[\alpha]_D$ +74° (*c* 3·5 in MeOH). A portion was hydrolysed by N-sulphuric acid at 100° for 2 hr. and the syrupy reducing sugars were isolated and chromatographed. The faster-moving component was identified as 2 : 3 : 4-tri-*O*-methyl-D-xylose, m. p. and mixed m. p. 85—87°, $[\alpha]_D$ +42° (7 min.) ⟶ +18° (80 min., constant). The derived 2 : 3 : 4-tri-*O*-methyl-*N*-phenyl-α-D-xylopyranosylamine had m. p. and mixed m. p. 103—105°.

The slower-moving component did not crystallise. It moved as one spot on paper chromatograms in all solvents used and had the same rate of movement as 2 : 3-di-*O*-methyl-D-xylose. It gave a brownish-red colour with the *p*-anisidine hydrochloride spray, whereas the 2 : 3- and 2 : 4-di-*O*-methyl derivatives both gave deep pink-red colours. The syrup was oxidised with bromine water, and the methylated xylonic acid was converted into the lactone by heating it at 90° under reduced pressure for 30 min. The lactone readily crystallised and, after recrystallisation from ether–*n*-hexane, had m. p. 68°, not depressed on admixture with 3 : 4-di-*O*-methyl-D-xylonolactone.

4-O-β-D-*Xylopyranosyl*-D-*xylose*.—Fraction C_3 crystallised and was recrystallised twice from moist ethanol. The crystals had m. p. 195—197°, undepressed on admixture with xylobiose obtained from aspen wood sawdust. On chromatograms, the two sugars were indistinguishable. They had $[\alpha]_D$ −40° (3 min.) ⟶ −27° (1 hr., constant; *c* 2·5). Both had the same *X*-ray powder photograph. The derived phenylosazone had m. p. and mixed m. p. 210—213° (decomp.).

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8. *The Kinetics and Mechanisms of Addition to Olefinic Substances. Part V.* Products of the Reaction between Bromine Chloride and Propene in Water.*

By P. B. D. DE LA MARE and S. GALANDAUER.

Addition of bromine chloride to propene in aqueous hydrochloric acid gives 1-bromo-2-chloropropane and 2-bromo-1-chloropropane in the proportion 54 : 46. A mixture of bromohydrins is also produced, in amount decreasing as the amount of chloride ions is increased. This mixture contains 1-bromopropan-2-ol and 2-bromopropan-1-ol in the proportion 79 : 21. These ratios do not change significantly when the chloride-ion concentration is changed from 1M to 3M. There was no indication of the production of dichloride or of chlorohydrin. The theoretical significance of these results is discussed.

MICHAEL[1] first recorded that, when bromine chloride or iodine chloride is added to propene, significant amounts of the 2-bromo- or 2-iodo-isomers are produced. For

* Part IV, *J.*, 1957, 1481.

[1] Michael, *J. prakt. chem.*, 1899, **60**, 450.

bromine chloride, it was recorded that the ratio of 1-bromo-2-chloropropane to 2-bromo-1-chloropropane was 58 : 42. This reaction was re-investigated by Stickler,[2] who gave a value of 80 : 20; his experimental details and conditions are not available to us.

For iodine chloride, Michael found the ratio of 2-chloro-1-iodopropane to 1-chloro-2-iodopropane to be 80 : 20. Ingold and Smith [3] repeated this estimation while studying orientation in such addition reactions, and obtained a value of 69 : 31.

The orientational and mechanistic significance attributable to the presence of the minor product of these reactions is obscured because the interhalogen compound might have acted as a donor of electrophilic chlorine rather than of bromine, *i.e.*, some reaction might have occurred through chlorine produced by the equilibrium $2BrCl \rightleftharpoons Cl_2 + Br_2$, or bromine chloride might have become polarised during the collision between the reactants in the sense $\overset{\delta+}{Cl}\text{–}\overset{\delta-}{Br}$. We have re-investigated this problem to examine these mechanistic possibilities.

Experimental

1-Bromo-2-chloropropane.—This was prepared by treating α-chloropropionic acid with thionyl chloride and reducing the α-chloropropionyl chloride with lithium aluminium hydride. The chlorohydrin, which was accompanied by much by-product of higher b. p., presumably a condensation product (*e.g.*, Me·CHCl·CO·O·CH_2·CHCl·Me), was brominated with phosphorus tribromide as recommended by Dewael; [4] the product (11% yield), repeatedly dried (P_2O_5) and distilled under reduced pressure, had b. p. 116—117°/760 mm., n_D^{25} 1·4740 (Found: C, 23·0; H, 3·9; Hal, 71·6 *. Calc. for C_3H_6ClBr: C, 22·8; H, 3·8; Hal, 73·1%).

The infrared spectrum is recorded in Table 1, together with those of related compounds, determined as thin films between rock-salt plates, by use of a Grubb-Parsons double-beam recording infrared spectrophotometer. Its isomer has characteristic peaks at 717 cm.$^{-1}$ and 741 cm.$^{-1}$, and these absorption bands do not appear, or at the worst appear only very weakly, in the spectrum of 1-bromo-2-chloropropane; thus the specimen was contaminated with less than 1—2% of the isomer.

2-Bromo-1-chloropropane.—Allyl chloride was treated with sulphuric acid, cupric sulphate, and water, the resulting chlorohydrin being brominated with phosphorus tribromide. The product (13% yield), repeatedly dried (P_2O_5) and distilled, had b. p. 116—117°/760 mm., n_D^{25} 1·4761 (Found: C, 23·4; H, 4·0; Hal, 73·2%). The infrared absorption spectrum (Table 1) shows that the specimen contained no isomeric bromochloropropanes, since absorption bands characteristic of the latter (*e.g.*, at 842, 671, 664, and 627 cm.$^{-1}$) are absent.

Analysis of Mixtures of 1-Bromo-2-chloropropane and 2-Bromo-1-chloropropane.—(i) *Infrared absorption.* The strong bands at 1151 cm.$^{-1}$ and 1163 cm.$^{-1}$, each characteristic of one isomer, appear in spectra of their mixtures as a double peak. Examination of mixtures containing 50—60% of the former isomer showed that the relative heights of the two peaks defined the composition to within about 0·5 unit per cent. This method was used, therefore for analysis of the products of reaction of bromine chloride with propene, as described below (Table 3).

(ii) *Kinetic methods.* The isomeric bromochloropropanes with sodium ethoxide in ethanol liberated acid at rates which were too similar for this method to be useful for kinetic analysis of mixtures, but rates of solvolysis in 50% ethanol were better separated. Samples of solutions in 50% ethanol (equal volumes of ethanol and water at room temperature) were sealed in tubes and heated at 99·9°. At intervals, the tubes were broken under ethanol containing perchloric acid, and the liberated halide ions titrated with silver nitrate potentiometrically, a silver wire being used as one electrode and a calomel half-cell as the reference electrode. Two end-points were obtained; the first, at 20—60 mv, represented liberation of bromide, and the second, at 220—260 mv, liberation of total halide. Values of the percentage of liberation of bromide,

* Bromine and chlorine being assumed present in equal proportion.

[2] Stickler, personal communication to G. W. Wheland, "Resonance in Organic Chemistry," John Wiley and Sons, 1955, p. 455.

[3] Ingold and Smith, *J.*, 1931, 2752.

[4] Dewael, *Bull. Soc. chim. belges*, 1930, **39**, 87.

calculated on the basis of the theoretical infinity value, were plotted against time. Table 2 gives values obtained from such graphs.

Mixture B clearly contains more 1-bromo-2-chloropropane than does mixture S; this

TABLE 1. *Infrared absorption bands (cm.$^{-1}$) of bromochloropropanes and of propylene bromohydrins.*

Me·CHCl·CH_2Br	Me·CHBr·CH_2Cl	Me·CH(OH)·CH_2Br	Me·CHBr·CH_2·OH
627 m	—	—	—
664 m	—	662 s	659 w
671 m	—	670 s	669 w
676 m	—	—	—
—	717 s	—	—
735 vw	741 m	—	—
—	—	792 w	—
842 w	—	821 m	—
857 w	859 w	858 w	858 w
893 m	871 w	873 m	879 w
—	878 w	—	892 w
905 m	900 m	935 s	915 w
986 m	—	978 w	978 m
993 m	998 s	—	—
1007 s	—	1033 s	1011 s
1034 m	—	1052 s	1028 s
1063 w	1063 s	1078 s	1057 s
1099 m	1106 w	—	1089 m
1117 m	1116 w	1134 s	1122 m
1171 s	1163 s	1190 m	1190 m
1220 s	1215 s	—	—
1227 s	—	1233 s	—
1245 m	1242 m	—	1250 m
1263 m	1264 m	1266 m	1263 m
—	1269 m	—	—
1309 m	1316 m	1300 m	1305 w
—	1335 w	1337 m	—
1372 s	1374 s	1381 s	1385 m
1416 m	—	—	—
1435 s	1431 s	1429 s	—
1443 s	1443 s	1458 m	1458 s
—	—	1650 w	—
2817 m	2825 m	2941 m	2941 s
2882 m	2882 m	2985 s	2976 m
2915 s	2933 s	3378 s	3344 s

s = strong; m = medium; w = weak; vw = very weak.

result (see Table 3) accords with the conclusion from infrared analysis. The first-order rate coefficients for the liberation of bromide, calculated on the above assumptions for the pure bromochloropropanes, were: 1-bromo-2-chloropropane, $k_1 = 4{\cdot}8 \times 10^{-5}$ min.$^{-1}$; 2-bromo-1-chloropropane, $k_1 = 18{\cdot}5 \times 10^{-5}$ min.$^{-1}$; these were substantially constant over 30—80% of reaction.

TABLE 2. *Hydrolytic liberation of bromide ions from bromochloropropanes in 50% ethanol at 99·9°.*

Liberation of Br^- (%)	20	30	40	50	60
Me·CHCl·CH_2Br; t (hr.)	85	150	200	270	320
Me·CHBr·CH_2Cl; t (hr.)	20	35	45	60	100
Mixture S *; t (hr.)	45	60	95	140	200
Mixture B *; t (hr.)	50	70	105	150	210

* S, Synthetic mixture, 50% of each isomer; B, sample from addition of bromine chloride to propene.

1-*Bromopropan*-2-*ol*.—Allyl bromide (140 g.) was added slowly to concentrated sulphuric acid (240 g.) containing copper sulphate (4 g.). The mixture was added cautiously to water and steam-distilled. The distillate was salted out with ammonium sulphate and extracted with

ether. The ether-extract was dried over ignited silica gel. Fractional distillation gave 1-bromopropan-2-ol (50 g.), b. p. 48—48·5°/13 mm., n_D^{25} 1·4772 (Found: C, 25·7; H, 5·1; Br, 57·1. Calc. for C_3H_7OBr: C, 25·7; H, 5·0; Br, 57·0%) (for infrared spectrum see Table 1). Although the material so prepared should be free from the isomer, the spectra suggest that it contains a trace of it, as shown, for example, by a very weak band at 978 cm.$^{-1}$, corresponding with the much more intense band there of 2-bromopropan-1-ol. The latter is more reactive in solvolysis, and kinetic analysis confirmed that the specimen of 1-bromopropan-2-ol was 94 ± 1% pure, and contained 6% of a more rapidly solvolysing impurity.

2-Bromopropan-1-ol.—The product of α-bromopropionic acid and thionyl chloride was reduced with lithium aluminium hydride to 2-bromopropan-1-ol (cf. ref. 5), which (20% yield) had b. p. 145°/758 mm., 45°/12 mm., n_D^{25} 1·4740 (Found: C, 26·1; H, 5·2; Br, 56·8%) (for infrared spectrum see Table 1). It appears to be quite free from its isomer (absence of strong band at 935 cm.$^{-1}$, characteristic of 1-bromopropan-2-ol).

Analysis of Mixtures of 1-Bromopropan-2-ol and 2-Bromopropan-1-ol.—Kinetic analysis was satisfactory since the rates of hydrolysis at 100·2° in initially neutral solution in water differed by a factor of about seven. The rate coefficient for the hydrolysis of 2-bromopropan-1-ol was $k_1 = 35·5 \times 10^{-3}$ min.$^{-1}$. The best sample of 1-bromopropan-2-ol prepared gave the following behaviour, portions (5·64 ml.) being titrated at intervals with 0·02057N-sodium hydroxide.

Time (min.)	0	20	40	60	90	130	170
Titre (ml.)	0·31	3·61	6·40	8·85	11·40	14·52	17·16
$\log_{10}(A - x)$	1·433	1·378	1·323	1·270	1·205	1·144	1·016
10^3k_1 (min.$^{-1}$)	—	—	—	—	—	5·35	5·57
Time (min.)	210	260	320	380	460	∞	
Titre (ml.)	19·05	21·28	22·80	23·91	25·51	27·45	
$\log_{10}(A - x)$	0·924	0·794	0·668	0·549	0·288	—	
10^3k_1 (min.$^{-1}$)	5·39	5·61	5·38	5·11	5·71	—	

The quoted values of the first-order rate-coefficients, k_1, are calculated by the usual formula, with $t = 90$ min. as the zero of time. For a mixture of isomers in total concentration A, if $\log_{10}(A - x)$ is plotted against time t, a curve is obtained, of limiting slope towards the conclusion of the reaction $-k_1/2·303$, where k_1 is the first-order rate coefficient for the less rapidly reacting isomer. Extrapolation of the best straight line through the later points gives an intercept of $\log_{10}a$ on the $A - x$ axis, where a is the concentration of the less rapidly reacting isomer. This treatment gives the mean rate coefficient as $5·45 \times 10^{-3}$ min.$^{-1}$, and demonstrates that the above sample is about 94% pure. There is present, therefore, about 6% of a more rapidly reacting impurity, presumably its isomer. Similar kinetic treatment of a synthetic mixture, containing 74·3% of 1-bromopropan-2-ol, gave 75·0% for the proportion of the less rapidly reacting isomer. This good accordance confirms this method of analysis.

Addition of Bromine Chloride to Propene.—Bromine chloride was prepared by adding the theoretical weight (37·8 g.) of bromine to a standardised solution (4 l.) of chlorine in 1·0M-hydrochloric acid. Propene, from a cylinder kindly given by Imperial Chemical Industries Limited, whom we thank, was passed through this solution in a dark vessel until all the bromine chloride was destroyed. The bromochloropropanes were extracted with pentane, and the extract was dried ($CaCl_2$) and distilled. There were recovered 4·3 g. (5·8%) of mixed bromochloropropanes, b. p. 116—118°/760 mm., 31·5—32°/30 mm., n_D^{25} 1·4740 (Found: C, 23·4; H, 4·0; Hal, 71·5%). To the aqueous residue after extraction with pentane was added ammonium sulphate to salt out the organic material, and the mixture was then extracted with ether to give 37·9 g. (58%) of mixed bromohydrins, b. p. 141—143°/760 mm., 45·5—49°/12 mm., n_D^{25} 1·4752 (Found: C, 26·0; H, 5·4; Br, 57·4%).

This experiment was repeated at other acidities. In no experiment was there any sign of material corresponding in b. p. or refractive index with either 1 : 2-dichloropropane or chlorohydrin. The total recovery in the best example was greater than 60%.

Analysis of the proportion of bromohydrin produced in the reaction was carried out as follows. A standardised solution of bromine chloride was prepared in aqueous hydrochloric acid. Propene was passed slowly through it until it was colourless. The solution was carefully neutralised with aqueous sodium hydroxide, care being taken to avoid local excess of alkali, with methyl-red as indicator. This removed the excess of hydrochloric acid, together with the acid produced in the reaction. Excess of standard sodium hydroxide was then added,

and the solution was left for some hours to destroy the bromohydrins. The solution was then back-titrated with hydrochloric acid. The following is a typical example. From a solution of bromine chloride (0·191M in 1·0N-hydrochloric acid), the bromohydrin liberated, on reaction with excess of alkali overnight, equalled 0·134N-acid. Hence 70% of bromohydrin is produced. Values for this and other experiments are given in Table 3, together with the results of analyses of the products isolated from the larger-scale experiments.

TABLE 3. *Products of reaction of bromine chloride with propene in aqueous hydrochloric acid.*

Concn. of HCl in reaction medium (M)	1·0	2·0	3·0
Bromohydrin formed (%)	70	60	51
1-Bromo-2-chloropropane in bromochloropropanes (%)	53·5	55	54
1-Bromopropan-2-ol in bromohydrins (%)	78·5	79	79

Bromo-olefins, which might have been formed by substitution, could have escaped detection in the recovery of the products, but separate experiments showed that these formed, at most, only a small proportion of the overall product. Propene was passed through a solution of bromine chloride in 0·050N-hydrochloric acid. At the end of the reaction, a portion (25 ml.) was titrated with 0·100N-alkali; the acid formed in the reaction, additional to the hydrochloric acid already present, was thus found to be 0·0177N. Excess of alkali was added, and after an appropriate time the mixture was back-titrated with acid; the bromohydrin had liberated 0·0162N-acid. The first figure represents the acid liberated by the two reactions:

$$Me{\cdot}CH{:}CH_2 + BrCl + H_2O \longrightarrow Me{\cdot}CH(OH){\cdot}CH_2Br\,^{*} + HCl$$

$$Me{\cdot}CH{:}CH_2 + BrCl \longrightarrow Me{\cdot}CH{:}CHBr + HCl$$

The second represents that liberated by the reaction:

$$Me{\cdot}CH(OH){\cdot}CH_2Br\,^{*} \xrightarrow{NaOH} Me{\cdot}\underset{\diagdown O \diagup}{CH}{\cdot}CH_2 + HBr$$

Hence, at most, the reaction which forms bromohydrin is accompanied by less than 10% of substitution. Repetition of the above experiment with added sodium chloride (1·7M) confirmed this conclusion.

DISCUSSION

It is a marked feature of these experiments that the amounts of 1-bromo-2-chloropropane and 2-bromo-1-chloropropane formed in the reaction between propene and bromine chloride are nearly equal. It is customary to consider electrophilic addition to such a compound as propene in terms of mechanisms involving carbonium-ionic intermediates, and there are various possibilities here.

Addition could possibly proceed by Scheme 1, interaction between the carbonium-ionic centre and the neighbouring halogen substituent being assumed but for the time being not formulated.

Scheme 1.

$$2BrCl \rightleftharpoons Br_2 + Cl_2$$

$$Br_2 + Me{\cdot}CH{:}CH_2 \xrightarrow{-Br^-} Me{\cdot}\overset{+}{C}H{\cdot}CH_2Br \xrightarrow{+Cl^-} Me{\cdot}CHCl{\cdot}CH_2Br$$

$$Cl_2 + Me{\cdot}CH{:}CH_2 \xrightarrow{-Cl^-} Me{\cdot}\overset{+}{C}H{\cdot}CH_2Cl \xrightarrow{+Br^-} Me{\cdot}CHBr{\cdot}CH_2Cl$$

In the present example, this can be excluded as a route to 2-bromo-1-chloropropane,

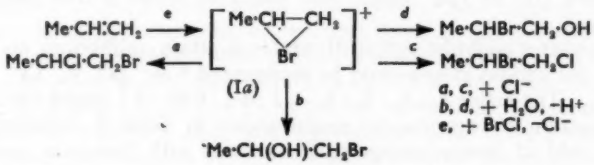
* And isomers.

for the concentration of chloride ion is so large, and so considerably exceeds that of bromide ion, that the final product of reaction through the cation $Me{\cdot}\overset{+}{C}H{\cdot}CH_2Cl$ would have to be 1 : 2-dichloropropane formed by attack of chloride ions in completion of the reaction.

Similar considerations can be used to eliminate the possibility that 2-bromo-1-chloropropane is obtained by attack on the olefin by bromine chloride polarised in the sense $Cl^{\delta+}-Br^{\delta-}$, or by Cl^+. The formation of bromochloropropane clearly involves a diversion by chloride ions of a reaction which would otherwise have produced bromohydrin, for the yield of bromochloride becomes greater as the concentration of chloride ions is increased. Furthermore, increase in the concentration of chloride ions in the medium, though it increases the total amount of bromochloropropane produced, has no effect on the ratio of isomers isolated in this fraction. We conclude that the intermediate involved in the formation of bromochloropropane and of bromohydrin has the empirical composition $[(Me{\cdot}CH{:}CH_2),\ (Br)]^+$, and is obtained by attack on the olefin of a carrier of electrophilic bromine, not of electrophilic chlorine.

There remain a number of possible paths and intermediates. Scheme 2 gives a simple representation.

Scheme 2.



This scheme involves the formation of only one intermediate, which has been represented in the bromonium [6] form (I*a*)* This then reacts bimolecularly with chloride ions, or with water, to form the various products. It requires that there is an intrinsic difference in the ratios [(1 : 0·85 and 1 : 0·25)] in which chloride ions and water molecules respectively attack the primary and secondary carbon atoms of the intermediate (I*a*). Furthermore, the former ratio must be considerably different from that [7] of attack by the same reagent on the analogous cation (I*b*) (1 : 0·33).

$\left[\begin{matrix} Me{\cdot}CH{\cdot}CH_2 \\ \diagdown\ \diagup \\ {}^+OH \end{matrix}\right]^+$ (I*b*)

Elsewhere, however, arguments have been adduced [8,9,10] to suggest that more than one type of intermediate must be concerned in some of these reactions, as for example in the additions of halogens to cholesterol and its derivatives [11] and of hypochlorous acid to olefins. It would not accord with the experimental results to assume here that, whereas the 2-bromo-products were obtained as in Scheme 2, the 1-bromo-compounds were obtained wholly or partly by a unimolecular ring-opening of the bromonium ion (I*a*), followed by reaction with a nucleophilic reagent; for if the unimolecular ring-opening were partly rate-determining, in competition with stages (*c*) and (*d*) of Scheme 2, then increase in the concentration of chloride ions would divert the reaction towards stage (*c*), the formation of $Me{\cdot}CHBr{\cdot}CH_2Cl$, at the expense of all the other products, and so the ratio

* It could equally be represented in the manner of (II), Scheme 3.

[5] Forsberg, *Acta Chem. Scand.*, 1954, **8**, 135.
[6] Roberts and Kimball, *J. Amer. Chem. Soc.*, 1937, **59**, 947.
[7] Smith and Skyle, *Acta Chem. Scand.*, 1950, **4**, 39.
[8] de la Mare, in " Progress in Stereochemistry," ed. Klyne, Butterworths, London, 1953, p. 118.
[9] de la Mare and Pritchard, *J.*, 1954, 3910, 3679.
[10] Ballinger and de la Mare, *J.*, 1957, 1481.
[11] Grob and Winstein, *Helv. Chim. Acta*, 1952, **35**, 782.

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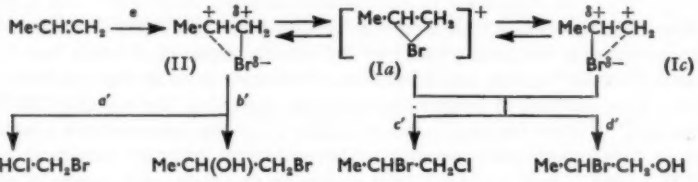
of isomeric bromochloropropanes would alter with the concentration of chloride ions. This is contrary to experimental fact.

An elaboration of Scheme 2, which we prefer, is shown in Scheme 3, and accords with that suggested [8] for the addition of iodine chloride to propene.

Scheme 3.



In this scheme (route letters analogous to Scheme 2), at least two intermediates are envisaged: the unsymmetrical carbonium ion (II), stereochemically held in or near the indicated geometry by electrostatic forces; and either the bromonium ion (I*a*) or the other unsymmetrical carbonium ion (I*c*). The latter, if it exists as a kinetic intermediate, must be separated from (II) by (I*a*), which then might be either a true intermediate or a transition state.

These intermediates might be sufficiently stable to attain equilibrium, and then react at rates which for the various stages could be represented * as: (*a'*), k_a . Cl^-; (*b'*), k_b; (*c'*), k_c . Cl^-; (*d'*), k_d. The ratios $k_a : k_b : k_c : k_d = 1 : 4{\cdot}4 : 0{\cdot}85 : 1{\cdot}1$ would then qualitatively reproduce the pattern of experimental results shown in Table 3, including the features that the total yield of bromochloropropane increases with increasing concentration of chloride ions, but that neither the ratio of isomeric bromochloropropanes nor that of the isomeric bromohydrins is altered by change in the concentration of chloride ions.

TABLE 4. *Proportion of product of attack on the* 1*-carbon atom in additions to olefins.*

Olefin	$Me{\cdot}CH{:}CH_2$	$HO{\cdot}CH_2{\cdot}CH{:}CH_2$	$ClCH_2{\cdot}CH{:}CH_2$	$BrCH_2{\cdot}CH{:}CH_2$
ClOH; 1-chloro-compound in chlorohydrin (%) [7,9]	91	73	30	—
BrOH; 1-bromo-compound in bromohydrin (%)	79 *	66 †	—	20 †
BrCl; 1-bromo-compound in bromochloride (%)	54	—	—	—
ICl; 1-iodo-compound in iodochloride (%) [3]	71	—	—	—

* Electrophilic reagent, BrCl; this paper. † Electrophilic reagent, BrOH; ref. 7.

It seems reasonable that intermediates (I) and (II) should differ in the ratios in which they react with chloride ions and with water, particularly should it turn out that the intermediate (I) is predominantly in the bromonium form (I*a*). Thus the fact that the ratio of isomeric bromohydrins is about 4 : 1 in favour of the 1-bromo-derivative, whereas that of the isomeric bromochloropropanes is much more nearly 1 : 1, is interpreted as showing the different nature of the two intermediates concerned in the addition.

In the corresponding earlier schemes [9,10,12] for addition of hypochlorous acid to olefins, equilibria involving intermediates analogous with (I*a*), (I*c*), and (II) are not fully established before other reactions of the ion set in. This does not introduce an inconsistency, for the facts known concerning the interaction between carbonium-ionic centres

* It is implied that these values of *k* take into account the equilibrium constant between intermediates (I) and (II).

[12] de la Mare and Salama, *J.*, 1956, 3337.

and neighbouring halogen[13] suggest that the interaction is much more powerful with bromine than with chlorine, and hence the present example would be expected to be more favourable than those studied previously for the establishment of such equilibria.

The change in orientation with change in structure of the olefin, noted previously for the addition of hypochlorous acid,[9] is paralleled in the addition of hypobromous acid, as shown in Table 4.

The change in orientation with change from electrophilic chlorine to electrophilic bromine is also quite regular, but the sequence is apparently not continued regularly with iodine. Such a discrepancy does not seem to have a natural explanation in terms of Scheme 2, but it could be interpreted through Scheme 3; for the ratio of products formed by routes *a'* and *c'* will depend on both the ratio of the appropriate rate coefficients and the equilibrium proportions of intermediates (I) and (II). It would be consistent with current views on interaction between neighbouring groups and carbonium-ionic centres (cf. ref. 13) that the proportion of form (I*a*) in equilibrium with (II) might be greatest for iodine (sequence I > Br > Cl), but that, because of this difference in stability, the ratio of rates of further reaction of forms like (II) and (I*a*) might be least for iodine (sequence I < Br < Cl). Such a combination could give the irregular sequence of product-composition noted for propene in Table 4; we hope to investigate this further.

Added, November 4th, 1957.—Traynham and Conte[14] have recently described the preparation of 1-bromo-2-chloropropane by the chlorination, with thionyl chloride, of the bromohydrin produced by the reaction of hydrogen bromide with propylene oxide. They state that the infrared spectrum of their product was similar to that of 2-bromo-1-chloropropane except for a medium-intensity band at 9·05 μ (1105 cm.$^{-1}$) not found in the latter. Their procedure would be expected to give a mixture of these two isomers, since the corresponding reaction of propylene oxide with hydrogen chloride gives a mixture of chlorohydrins.[7] In our experience, the former compound is better distinguished by the bands at 1034 and 842 cm.$^{-1}$, the latter by the bands at 717, 741, and 1063 cm.$^{-1}$ (Table 1). Traynham and Conte do not describe their source of 1-chloropropan-2-ol, from which their 2-bromo-1-chloropropane was obtained; their spectrum, as far as they record it, accords qualitatively with that which we report for either isomer, their scale of wavelength being shifted with respect to ours by about +5 cm.$^{-1}$ These considerations clearly have relevance to their discussion of the possibility of migration of chlorine to the 2-position during the addition of hydrogen chloride to 3-chloropropene.

We are indebted to Dr. P. Ballinger for help with the infrared measurements and to Mr. C. Bilby for technical assistance. The continued interest of Professor E. D. Hughes, F.R.S., and of Professor C. K. Ingold, F.R.S., is greatly appreciated.

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University College, London, W.C.1. [*Received, July 25th,* 1957.]

[13] Cf. Winstein, *Bull. Soc. chim. France,* 1951, **18**, C55.
[14] Traynham and Conte, *J. Org. Chem.,* 1957, **22**, 702.

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9. *The Oxidation of Aromatic Amines. Part VI.* Persulphate Oxidation of Some Carcinogenic Aromatic Amines.*

By Peter Sims.

The action of alkaline persulphate on a number of aromatic amines, most of which are carcinogenic, gives, as principal products, the sulphuric esters of the corresponding *o*-aminophenols, which yield the free *o*-aminophenols on acid-hydrolysis.

The results of Bonser, Clayson, Jull, and Pyrah [1] suggest that the carcinogenic action of 2-naphthylamine may be due, not to the amine itself, but to 2-amino-1-naphthol formed by the metabolism of the amine in the body. Other carcinogenic aromatic amines may act *via* the corresponding *o*-aminophenols, and in order to test this by the method of bladder implantation [2,3] small amounts of the *o*-aminophenols were required. Many of these aromatic amines can be oxidised with alkaline persulphate in the manner previously described [4,5] to give reasonable yields of the corresponding aminophenyl sulphuric esters, which yield the aminophenols on acid-hydrolysis. The sulphuric esters and, in most cases, the aminophenols are new compounds, and in some cases it has not been possible to establish their identity unequivocally. In the aromatic series, only *o*-carboxy-amines are substituted in the *para*-position to the amino-group by the entering sulphuric ester group; [6] *meta*-substituted products have never been detected. Most of the amines which we oxidised are already *para*-substituted and we have assumed therefore that the products are *ortho*-substituted amines. The amines successfully oxidised in this reaction were 2′-chloro-4-dimethylamino- and 4-dimethylamino-2′-methyl-*trans*-stilbene, 4-dimethylamino-azobenzene and -diphenyl, *NN*-dimethyl-1- and -2-naphthylamine, 3 : 4 : 1-xylidine, and sulphanilamide.

With the stilbenes some oxidation of the double bonds occurred: *o*-chloro- and *p*-dimethylamino-benzoic acid, and *o*-toluic acid, were isolated. 4-Dimethylaminostilbene itself was scarcely attacked by persulphate, the only product isolated being a little benzoic acid. The ultraviolet spectra of the sulphuric esters and aminophenols derived from the substituted dimethylaminostilbenes confirmed the proposed structures (Roe, unpublished work) and were similar to that of 4-amino-3-methoxystilbene.[7] The presence of small amounts of substituted 4-dimethylamino-*cis*-stilbenes was also indicated.

Persulphate oxidations of 2-aminofluorene and 4-amino-4′-fluorodiphenyl (which yielded brown amorphous substances), 2-amino-anthracene, -anthraquinone, and -chrysene, and 4-aminoazobenzene (which failed to react to any appreciable extent) were unsuccessful. 4 : 4′-Diaminodiphenyl sulphone, 2-amino-2′ : 3-dimethylazobenzene, and di-2′-chloroethyl-2-naphthylamine yielded sulphuric esters which did not crystallise.

Of the *o*-aminophenols isolated, 2-amino-4 : 5-dimethylphenol [3] and 4-dimethylamino-3-hydroxyazobenzene (unpublished observations) induced cancer of the bladder when implanted into the bladders of mice. Tested under the same conditions 4-dimethylamino-3-hydroxydiphenyl and 1-dimethylamino-2-naphthol were not carcinogenic. The biological tests on the other aminophenols are not yet complete.

It is of interest that, whereas 4-dimethylaminostilbene was not attacked by persulphate,

* Part V, Boyland and Manson, *J.*, 1957, 4689.

[1] Bonser, Clayson, Jull, and Pyrah, *Brit. J. Cancer*, 1952, **6**, 412.
[2] *Idem*, *ibid.*, 1956, **10**, 533; Bonser, Bradshaw, Clayson, and Jull, *ibid.*, p. 539.
[3] Boyland and Watson, *Nature*, 1956, 177, 837; Allen, Boyland, Dukes, Horning, and Watson, *Brit. J. Cancer*, 1957, **11**, 212.
[4] Boyland, Manson, and Sims, *J.*, 1953, 3622.
[5] Boyland and Sims, *J.*, 1954, 980.
[6] Boyland, Sims, and Williams, *Biochem. J.*, 1956, **62**, 546.
[7] Bergel, *Chem. and Ind.*, 1954, 904.

the 2′-chloro- and the 2′-methyl derivative were oxidised. These substituted 4-dimethylaminostilbenes are more active as growth-inhibitors and carcinogens than 4-dimethyl aminostilbene itself. The compounds which are the more susceptible to persulphate oxidation are the more active biologically.

Experimental

Materials.—The aminostilbenes had been prepared by the methods of Haddow, Harris, Kon, and Roe.[8] *NN*-Dimethyl-2-naphthylamine, m. p. 46°, and 4-dimethylaminodiphenyl, plates (from ethanol), m. p. 120° (lit.,[9] m. p. 123°) (Found: C, 85·3; H, 7·6; N, 7·4. Calc. for $C_{14}H_{15}N$: C, 85·2; H, 7·7; N, 7·1%), were prepared in good yield from the unmethylated amines with trimethyl phosphate.[10] The other amines were commercial products.

Persulphate Oxidations.—The amines, in aqueous-acetone solution, were treated with a 10% excess of sodium or potassium persulphate in the presence of a 20% excess of aqueous sodium or potassium hydroxide as previously described,[4,5] except that with the tertiary amines the persulphate was added as a solid at the beginning of the oxidations. The mixtures were stirred at room temperature for 8 hr., kept overnight, filtered, and treated as described below.

2′-Chloro-4-dimethylamino-trans-*stilbene.* The solution obtained from the oxidation of the amine (10 g.) was evaporated to 200 ml. under reduced pressure, and the unchanged amine (5·2 g.) filtered off. The filtrate was washed with ether for 4 hr. and the aqueous phase evaporated to 25 ml. under reduced pressure. The solid was filtered off and recrystallised from water, to yield the *sodium salt* of the sulphuric ester in yellow plates (Found: after drying at 25°/0·5 mm: N, 3·7; Cl, 9·0; S, 7·95. $C_{16}H_{15}O_4NClSNa,H_2O$ requires N, 3·6; Cl, 9·0; S, 8·1%). The filtrate was acidified with 2N-sulphuric acid and extracted with ether (3 × 100 ml.), the ethereal solution was extracted with aqueous sodium hydrogen carbonate (2 × 5 ml.), and the aqueous solution was washed with ether and acidified with 2N-sulphuric acid. The solution was kept overnight at 0°, and the solid (23 mg.) filtered off and crystallised from water in needles, to yield *p*-dimethylaminobenzoic acid, m. p. 232—233° (lit.,[11] m. p. 236°). The filtrate was extracted with ether (3 × 50 ml.), and the ether was evaporated to leave a gummy solid which was extracted with boiling light petroleum (b. p. 80—100°). Removal of the solvent afforded a solid (230 mg.), m. p. 130—133°; after three recrystallisations from water it formed needles, m. p. 139—140°, undepressed in admixture with *o*-chlorobenzoic acid.

When a suspension of the sodium salt of the sulphuric ester in water was acidified with concentrated hydrochloric acid, a gum was formed which rapidly crystallised to yield the *sulphuric ester* of 2′-chloro-4-dimethylamino-3-hydroxy-*trans*-stilbene in needles (from aqueous ethanol), m. p. 220—224° (decomp.) (Found: C, 54·4; H, 4·9; N, 3·8; S, 8·7. $C_{16}H_{16}O_4NClS$ requires C, 54·5; H, 4·6; N, 4·0; S, 9·1%). Solutions of the ester had a bright blue fluorescence in ultraviolet light.

The ester (2 g.), suspended in water (50 ml.) and concentrated hydrochloric acid (10 ml.), was heated to 100° for 30 min. A slight excess of aqueous sodium hydrogen carbonate was added to the cooled solution, *2′-chloro-4-dimethylamino-3-hydroxy*-trans-*stilbene* (1·25 g.) separating. From aqueous ethanol or from ethyl acetate it formed flat greenish needles, m. p. 137—138° (Found: C, 70·0; H, 6·1; N, 5·2. $C_{16}H_{16}ONCl$ requires C, 70·2; H, 5·9; N, 5·1%). On sublimation at 120—170°/0·2 mm. it formed colourless plates, m. p. 139—139·5°. The aminophenol had a bright blue fluorescence in ultraviolet light.

4-Dimethylamino-2′-methyl-trans-*stilbene.* When this amine (10 g.) was treated as described above, unchanged starting material (4·9 g.) was recovered. The crude sodium salt (3·6 g.) obtained was suspended in water (25 ml.) and acidified with 10N-sulphuric acid; the *sulphuric ester* of 4-dimethylamino-3-hydroxy-2′-methyl-*trans*-stilbene (3·2 g.) separated as a gum which crystallised; from aqueous ethanol it formed needles, m. p. 183—185° (Found: C, 61·3; H, 5·85; N, 4·4; S, 9·8. $C_{17}H_{19}O_4NS$ requires C, 61·2; H, 5·7; N, 4·2; S, 9·6%). The *sodium salt* (Found: N, 3·7; S, 8·6. $C_{17}H_{18}O_4NSNa$ requires N, 3·95; S, 9·0%) and *potassium salt* (Found: N, 3·85. $C_{17}H_{18}O_4NSK$ requires N, 3·8%) (prepared from the acid) separated from water in pale yellow feathery needles and yellow plates respectively. Solutions of the ester had a bright

[8] Haddow, Harris, Kon, and Roe, *Phil. Trans.*, 1948, *A*, **241**, 147.
[9] Bell and Kenyon, *J.*, 1926, 2709.
[10] Billman, Radike, and Mundy, *J. Amer. Chem. Soc.*, 1942, **64**, 2977.
[11] Harben and Freund, *Ber.*, 1909, **42**, 4815.

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blue fluorescence in ultraviolet light. *o*-Toluic acid (165 mg.) was isolated from the mother-liquors from the oxidation in the way already described, separating from water in needles, m. p. and mixed m. p. 101—102°.

The ester (2 g.) was hydrolysed with concentrated hydrochloric acid, to yield *4-dimethylamino-3-hydroxy-2'-methyl*-trans-*stilbene* (1·3 g.); from aqueous ethanol it formed light brown plates, m. p. 153·5—154·5° (Found: C, 80·3; H, 7·7; N, 5·7. $C_{17}H_{19}ON$ requires C, 80·6; H, 7·6; N, 5·5%). The aminophenol sublimed at 130°/0·2 mm., as colourless plates, m. p. 153·5—154·5°. Solutions of the aminophenol had a strong blue fluorescence in ultraviolet light.

4-Dimethylaminoazobenzene. The amine (10 g.) was treated with potassium persulphate in the usual manner. When the reaction mixture was evaporated to 200 ml. under reduced pressure, unchanged amine (9·2 g.) separated. The filtrate was washed with ether and evaporated to 10 ml. under reduced pressure, the *potassium salt* (510 mg.) of the sulphate ester separating. It crystallised from methanol–ether in orange plates and from water in golden-yellow plates (Found: C, 47·1; H, 4·2; N, 11·6; S, 8·9. $C_{14}H_{14}O_4N_3SK$ requires C, 46·8; H, 3·9; N, 11·7; S, 8·9%).

When the potassium salt was suspended in water and acidified with hydrochloric acid, the *sulphuric ester* of 4-dimethylamino-3-hydroxyazobenzene separated; from aqueous ethanol it formed red plates, decomp. 195—198° (Found: C, 52·7; H, 5·0; N, 13·1; S, 9·7. $C_{14}H_{15}O_4N_3S$ requires C, 52·3; H, 4·7; N, 13·1; S, 10·0%). Hydrolysis of the ester with hydrochloric acid as before afforded *4-dimethylamino-3-hydroxyazobenzene*, separating from light petroleum (b. p. 80—100°) in feathery golden-yellow needles, m. p. 131—131·5° (Found: C, 69·8; H, 6·45; N, 17·6. $C_{14}H_{15}ON_3$ requires C, 69·7; H, 6·3; N, 17·4%).

4-Dimethylaminodiphenyl. 4-Dimethylaminodiphenyl (10 g.) was oxidised with sodium persulphate and the reaction mixture was treated in the usual manner. *Sodium 4-dimethylamino-3-diphenylyl sulphate* (3·3 g.) separated: from water it formed plates (Found: N, 4·6. $C_{14}H_{14}O_4NSNa$ requires N, 4·4%). When a suspension of the salt in water was acidified with concentrated hydrochloric acid *4-dimethylamino-3-diphenylyl hydrogen sulphate* separated which crystallised from ethanol in elongated plates, m. p. 228—231° (decomp.) (Found: C, 57·2; H, 5·2; N, 4·7; S, 10·8. $C_{14}H_{15}O_4NS$ requires C, 57·3; H, 5·1; N, 4·8; S, 10·9%).

The ester (1·2 g.) was hydrolysed as before, to yield *4-dimethylamino-3-hydroxydiphenyl* (0·85 g.), separating from aqueous ethanol in flat needles, m. p. 128—129° (Found: C, 78·6; H, 7·1; N, 6·7). $C_{14}H_{15}ON$ requires C, 78·8; H, 7·1; N, 6·6%).

NN-*Dimethyl-1-naphthylamine.* The amine (10 g.) was oxidised as before and the reaction mixture evaporated to 200 ml. under reduced pressure and washed with ether. The pH of the aqueous solution was adjusted to 4 with 2N-sulphuric acid, and the mixture was washed with ether; the brown gum, which first separated, crystallised. *1-Dimethylamino-2-naphthyl hydrogen sulphate* (2·9 g.) was purified by dissolving it in aqueous sodium hydrogen carbonate and acidifying the solution with concentrated hydrochloric acid; it formed plates, m. p. 155—158° (decomp.) (Found: N, 5·25; S, 12·3. $C_{12}H_{13}O_4NS$ requires N, 5·2; S, 12·0%). The *sodium salt* (prepared from the acid) separated from ethanol–ether in pinkish plates (Found: N, 4·7; S, 11·1. $C_{12}H_{12}O_4NSNa$ requires N, 4·8; S, 11·1%). The ester was hydrolysed with hydrochloric acid in the usual manner, the solution was treated with a slight excess of sodium hydrogen carbonate, and the product was isolated with ether. 1-Dimethylamino-2-naphthol crystallised from aqueous ethanol in needles, m. p. 52—53° (lit.,[11] m. p. 54°) (Found: C, 76·6; H, 7·1; N, 7·5. Calc. for $C_{12}H_{13}ON$: C, 77·0; H, 7·0; N, 7·5%). The *benzoyl derivative* separated from aqueous ethanol in needles, m. p. 70—71° (Found: C, 77·9; H, 5·9; N, 4·8. $C_{19}H_{17}O_2N$ requires C, 78·3; H, 5·9; N, 4·8%).

NN-*Dimethyl-2-naphthylamine.* The amine (10 g.) was similarly oxidised, yielding *2-dimethylamino-1-naphthyl hydrogen sulphate* (3·7 g.), plates (from 90% aqueous ethanol), m. p. 172—174° (softening at 152°) (Found: C, 53·9; H, 4·9; N, 5·3; S, 12·15. $C_{12}H_{13}O_4NS$ requires C, 53·9; H, 4·9; N, 5·2; S, 12·0%). The ester was hydrolysed with hydrochloric acid in the usual manner to yield a solid which was distilled in a microsublimation apparatus at 65°/0·1 mm. to yield plates, m. p. 33—34°, which rapidly decomposed in air and are presumed to be 2-dimethylamino-1-naphthol. The solid yielded a *benzoyl derivative* which separated from light petroleum (b. p. 80—100°) in pale orange needles, m. p. 111—113° (Found: C, 78·0; H, 5·8; N, 4·9. $C_{19}H_{17}O_2N$ requires C, 78·3; H, 5·9; N, 4·8%).

3 : 4 : 1-*Xylidine.* The amine (10 g.) was oxidised with sodium persulphate, and the reaction

[11] Haworth, Lamberton, and Woodcock, *J.*, 1947, 182.

mixture was treated in the usual manner and finally evaporated to dryness under reduced pressure. The residue was extracted with boiling methanol (3 × 100 ml.), and the combined extracts evaporated to small volume and kept at room temperature overnight. *Sodium 2-amino-4 : 5-dimethylphenyl sulphate* (4·2 g.) was obtained; from aqueous ethanol it formed flat, light brown needles (Found: N, 5·6. $C_8H_{10}O_4NSNa$ requires N, 5·9%). The *hydrogen sulphate* (obtained by acidification of an aqueous solution of the sodium salt) crystallised from ethanol in needles, m. p. 254—257° (decomp.) (Found: C, 44·1; H, 5·2; N, 6·4. $C_8H_{11}O_4NS$ requires C, 44·2; H, 5·1; N, 6·45%). The *potassium salt* (prepared from the acid) separated from aqueous ethanol in plates (Found: N, 5·6. $C_8H_{10}O_4NSK$ requires N, 5·5%).

Acid-hydrolysis of the ester (2 g.) yielded 2-amino-4 : 5-dimethylphenol (1·35 g.), separating from ether in light brown plates, m. p. 169—171° (Found: N, 10·6. Calc. for $C_8H_{11}ON$: N, 10·2%). The aminophenol was purified by sublimation at 170°/0·2 mm., forming colourless plates, m. p. 174—175°, which reddened in air (lit.,[13] m. p. 173—175°, becoming brown at 165°).

Sulphanilamide. Sulphanilamide (10 g.) was oxidised with potassium persulphate as before. The mixture was evaporated to 200 ml. under reduced pressure, filtered, washed with ether, and acidified to pH 3 with 2N-sulphuric acid. The coloured precipitate was separated, and the pH of the filtrate was adjusted to 7 with aqueous 2N-potassium hydroxide. The solution was evaporated to dryness under reduced pressure and the residue was extracted with boiling methanol (5 × 100 ml.). The combined extracts were evaporated to dryness, the residue was dissolved in a little water, and the solution was passed through a column of De-Acidite E ion-exchange resin (5 × 25 cm.), which absorbed most of the sulphuric ester together with some coloured material. The column was washed with methanol, and the ester eluted with aqueous 2N-ammonia (1 l.). The eluate was evaporated to dryness under reduced pressure, the residue was dissolved in boiling methanol (50 ml.), and coloured material was precipitated from the solution by means of ether (50 ml.). Excess of ether was added to precipitate the ammonium salt of the sulphate ester (3·75 g.), which separated as a gum which crystallised. Repeated recrystallisation of the product from methanol–ether afforded *ammonium 2-amino-p-sulphamoylphenyl sulphate* as reddish-brown needles (Found: C, 25·75; H, 3·9; N, 14·2; S, 22·6. $C_8H_{11}O_8N_3S_2$ requires C, 25·3; H, 3·9; N, 14·7; S, 22·5%).

When an aqueous solution of the ammonium salt was acidified with hydrochloric acid, *2-amino-*p*-sulphamoylphenyl hydrogen sulphate* separated. It was purified by dissolving it in aqueous sodium hydrogen carbonate and acidifying the solution; it formed pinkish plates, decomp. 245—248° (softening at 220°) (Found: C, 26·8; H, 3·2; N, 10·5. $C_8H_9O_8N_3S_2$ requires C, 26·9; H, 3·0; N, 10·4%). The ester separated from methanol–ether in pink solvated plates, m. p. 200—202° (decomp.) (Found, after drying at 100°/0·2 mm. for 4 hr.: C, 28·7, 28·8; H, 4·35, 4·0; N, 9·4, 9·1; S, 21·6. Calc. for $C_8H_9O_4N_3S_2,CH_3{\cdot}OH$: C, 29·0; H, 4·0; N, 9·3; S, 21·35%).

The ester was hydrolysed with hydrochloric acid as before and the solution was neutralised with sodium hydrogen carbonate and extracted with ether for 6 hr. The ether was removed and the residue crystallised from ethanol–chloroform, as described by Thorpe and Williams, in pinkish needles, m. p. 162—163°, undepressed on admixture with 4-amino-3-hydroxybenzenesulphonamide [14] (kindly supplied by Dr. W. V. Thorpe) (Found: N, 15·1. Calc. for $C_6H_8O_3N_2S$: N, 14·9%). When the aminophenol, in aqueous sodium hydroxide or in pyridine, was treated with an excess of benzoyl chloride a *tribenzoyl derivative* was formed, crystallising from aqueous ethanol in feathery needles, m. p. 222° (Found: C, 64·5; H, 4·0; N, 5·6. $C_{27}H_{20}O_6N_2S$ requires C, 64·8; H, 4·0; N, 5·6%); this (m. p. and mixed m. p. 222°) was also obtained when authentic 4-amino-3-hydroxybenzenesulphonamide was similarly treated (Found: C, 64·5; H, 4·1; N, 5·9%).

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[13] Crossley and Bartlett, *J.*, 1913, 1299.
[14] Thorpe and Williams, *Biochem. J.*, 1941, **35**, 61.

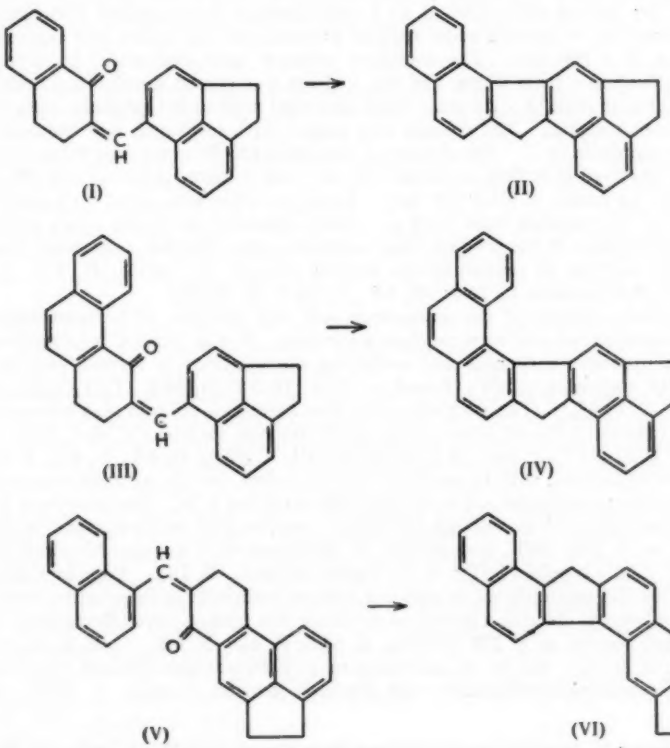
XUM

10. *The Synthesis of Some Hexa-, Hepta-, and Octa-cyclic Hydrocarbons Derived from Fluorene.*

By G. Saint-Ruf, Ng. Ph. Buu-Hoï, and P. Jacquignon.

Condensed polycyclic hydrocarbons containing fluorene and acenaphthene or pyrene nuclei have been prepared by cyclodehydration of the appropriate polycyclic arylidene-α-tetralones.

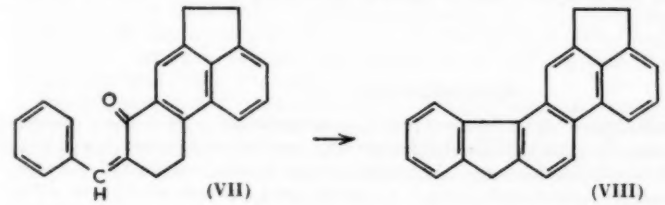
1 : 2-5 : 6-Dibenzofluorene is known to act as a biological antagonist of carcinogenic hydrocarbons such as 20-methylcholanthrene,[1] an effect which has been attributed to competitive fixation on cell proteins.[2] 1 : 2-5 : 6-Dibenzofluorene also exhibits strong inhibitory effects on the growth of grafted tumours in mice,[3] whilst its tumour-producing activity is of a very low order.[4] As part of a general study of the inhibition of



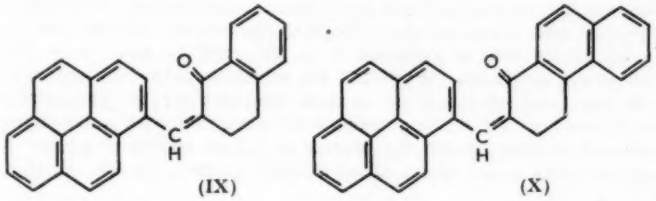
carcinogenesis, further polycyclic hydrocarbons of the same type were investigated, and this paper reports the synthesis of a number of hexa-, hepta-, and octa-cyclic fluorene derivatives containing also an acenaphthene or a pyrene ring.

[1] Lacassagne, Buu-Hoï, and Cagniant, *Compt. rend. Soc. biol.*, 1944, **138**, 16.
[2] Lacassagne, Buu-Hoï, and Rudali, *Brit. J. Expt. Path.*, 1945, **26**, 5; Buu-Hoï, *Arzneimittel-Forschung*, 1954, **4**, 531.
[3] Badger, Elson, Haddow, Hewett, and Robinson, *Proc. Roy. Soc.*, 1942, **130**, *B*, 255.
[4] Cf. Badger, Cook, Hewett, Kennaway, Kennaway, Martin, and Robinson, *Proc. Roy. Soc.*, 1940, **129**, *B*, 439.

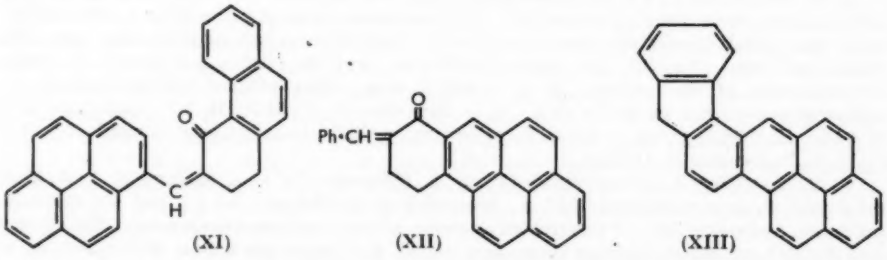
Rapson and Shuttleworth showed that 2-benzylidene-1 : 2 : 3 : 4-tetrahydro-1-oxonaphthalene undergoes cyclodehydration to 3 : 4-benzofluorene,[5] and the mechanism of this reaction was elucidated later by Buu-Hoï and Cagniant,[6] who extended the method to the synthesis of a number of more condensed fluorenes.[7] This reaction has now been applied to 2-(3-acenaphthenylmethylene)-1 : 2 : 3 : 4-tetrahydro-1-oxonaphthalene (I)



(VII) (VIII)

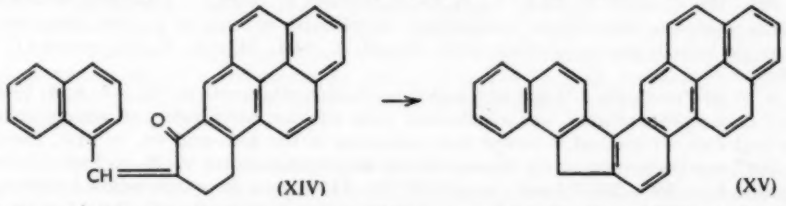


(IX) (X)



(XI) (XII) (XIII)

(prepared by condensation of acenaphthene-3-aldehyde with α-tetralone), which furnished in good yield, the hexacyclic compound (II); similarly, 3-(3-acenaphthenylmethylene)-1 : 2 : 3 : 4-tetrahydro-4-oxophenanthrene (III) gave the heptacyclic hydrocarbon (IV),



(XIV) (XV)

which has the surprisingly low m. p. of 138°, compared with that (228°) of its simpler analogue (II). Isomeric with the hydrocarbon (IV) is the compound (VI) obtained by cyclodehydration of the ketone (V), itself prepared by condensation of 1-naphthaldehyde with 1 : 2 : 3 : 4-tetrahydro-1-oxoacephenanthrene; the similar but simpler compound (VIII) was formed analogously in lower yield.

[5] Rapson and Shuttleworth, *J.*, 1940, 636.
[6] Buu-Hoï and Cagniant, *Rev. sci.*, 1943, **81**, 30.
[7] Buu-Hoï and Cagniant, *ibid.*, 1942, **80**, 319, 384, 436.

In the pyrene series, the ketones (IX), (X), and (XI) did not undergo cyclodehydration, but the reaction was successful with compounds (XII) and (XIV), which gave respectively the heptacyclic (XIII) and octacyclic (XV). These last two, yellow hydrocarbons are of especial interest, since they can be considered as substitution products of the highly carcinogenic 3 : 4-benzopyrene.

Results of tests for carcinogenic and/or tumour inhibitory effects will be reported elsewhere.

Experimental

2-(3-*Acenaphthenylmethylene*)-1 : 2 : 3 : 4-*tetrahydro*-1-*oxonaphthalene* (I).—The recorded method [8] for the preparation of acenaphthene-3-aldehyde was modified as follows: A solution of acenaphthene (50 g.) and dimethylformamide (27 g.) in dry xylene (100 c.c.) was heated on a water-bath for 6 hr. with phosphorus oxychloride (55 g.), a concentrated aqueous solution of sodium acetate in excess was added, and the mixture refluxed for 30 min. After cooling, the aldehyde was taken up in benzene, washed with water, and dried (Na_2SO_4), the solvent removed, and the residue fractionated *in vacuo*, giving 30% of aldehyde, b. p. 207—208°/15 mm., m. p. 88°. A mixture of this aldehyde (5 g.), α-tetralone (4 g.), and 4% ethanolic potassium hydroxide (50 c.c.) was shaken for 30 min., and left for 36 hr. at room temperature; the precipitated crystalline mass was collected, washed with dilute aqueous acetic acid, then with water, dried, and recrystallised from ethanol–benzene, giving the *product* as yellow leaflets (5 g.), m. p. 166°, dissolving in sulphuric acid with a deep violet colour (Found: C, 89·0; H, 5·9. $C_{23}H_{18}O$ requires C, 89·0; H, 5·8%).

3 : 3′-*Dimethylene*-1 : 2-5 : 6-*dibenzofluorene* (II).—A solution of the foregoing ketone (4·3 g.) in dry xylene (50 c.c.) was refluxed with phosphoric oxide (4 g.) for 30 hr.; after cooling, water was added, the organic layer washed with dilute aqueous sodium hydroxide, then with water, and dried (Na_2SO_4), the xylene distilled off, and the residue fractionated *in vacuo*. Crystallisation of the portion, b. p. >250°/1 mm., from ethanol–benzene yielded the colourless *hydrocarbon* as needles (1 g.), m. p. 228° (Found: C, 94·3; H, 5·7. $C_{23}H_{16}$ requires C, 94·5; H, 5·5%), giving a *dipicrate*, prisms, m. p. 199° (from benzene) (Found: N, 11·5. $C_{35}H_{22}O_{14}N_6$ requires N, 11·2%).

3 : 3′-*Dimethylene*-1 : 2-*benzonaphtho*(1″ : 2″-5 : 6)*fluorene* (IV).—A mixture of 1 : 2 : 3 : 4-tetrahydro-4-oxophenanthrene [9] (3·5 g.), acenaphthene-5-aldehyde (3·3 g.), and 4% ethanolic potassium hydroxide (50 c.c.) was treated as above, giving a red amorphous resin. The ethanol was distilled off, dilute aqueous acetic acid added, and the crude ketone (III) taken up in benzene; the benzene solution was washed with water and dried (Na_2SO_4), the solvent removed, and the residue dissolved in xylene (40 c.c.). The xylene solution was then refluxed for 30 hr. with phosphoric oxide (4 g.), and the product worked up as for (II). The portion of b. p. >260°/0·5 mm. was treated in benzene with picric acid, giving a *dipicrate*, brick red prisms, m. p. 195—196° (Found: N, 10·4. $C_{39}H_{24}O_{14}N_6$ requires N, 10·5%). Treatment with aqueous ammonia yielded a *hydrocarbon*, crystallising as yellowish prisms, m. p. 138°, from ethanol–benzene (no halochromy in sulphuric acid) (Found: C, 94·4; H, 5·4. $C_{27}H_{18}$ requires C, 94·7; H, 5·3%).

7 : 8 : 9 : 10-*Tetrahydro*-8-(1-*naphthylmethylene*)-7-*oxoacephenanthrene* (V).—7 : 8 : 9 : 10-Tetrahydro-7-oxoacephenanthrene was synthesised from succinic anhydride and acenaphthene by Fieser and Peters's method,[10] except that reduction of the keto-acid (m. p. 214°, instead of m. p. 208°) was performed by the Huang-Minlon modification of the Wolff–Kishner reaction; [11] the ketone, b. p. 250—256°/16 mm., m. p. 148° (lit., 147°), gave an orange-yellow halochromy in sulphuric acid. Treatment of this ketone (3·5 g.) with 1-naphthaldehyde (2·8 g.) in the usual way, afforded immediately a crystalline *product*, which formed pale yellow leaflets (3·5 g.), m. p. 220° (ethanol–benzene), giving a deep violet halochromy in sulphuric acid (Found: C, 90·3; H, 5·6. $C_{27}H_{20}O$ requires C, 90·0; H, 5·6%).

1 : 2-*Benzoacenaphtheno*(2′ : 3′-5 : 6)*fluorene* (VI).—A solution of the foregoing ketone (3 g.) in

[8] Cf. Fieser and Herschberg, *J. Amer. Chem. Soc.*, 1938, **60**, 2542.
[9] Buu-Hoï and Saint-Ruf, *J.*, 1957, 3806.
[10] Fieser and Peters, *J. Amer. Chem. Soc.*, 1932, **54**, 4347.
[11] Huang-Minlon, *ibid.*, 1946, **68**, 2487.

xylene (50 c.c.) was refluxed with phosphoric oxide (2·4 g.) for 30 hr.; the mixture, worked up in the usual way, afforded a *hydrocarbon*, yellowish needles (1·2 g.), m. p. 231° (from ethanol–benzene) (Found: C, 94·4; H, 5·5. $C_{27}H_{18}$ requires C, 94·7; H, 5·3%). The *picrate* crystallised as red leaflets, m. p. 211—212° (decomp. >180°), from benzene (Found: N, 7·0. $C_{33}H_{21}O_7N_3$ requires N, 7·4%).

8-*Benzylidene*-7 : 8 : 9 : 10-*tetrahydro*-7-*oxoacephenanthrene* (VII).—This *product*, prepared from 7 : 8 : 9 : 10-tetrahydro-7-oxoacephenanthrene (3·5 g.), benzaldehyde (1·7 g.), and 4% ethanolic potassium hydroxide (50 c.c.), crystallised as pale yellow leaflets (3·5 g.), m. p. 169°, from ethanol, giving a blood-red halochromy with sulphuric acid (Found: C, 88·8; H, 6·2. $C_{23}H_{16}O$ requires C, 89·0; H, 5·9%).

Acenaphtheno(3′ : 2′-3 : 4)*fluorene* (VIII).—This *hydrocarbon*, prepared from the foregoing ketone (2·5 g.), formed colourless prisms (0·8 g.), m. p. 209°, from ethanol–benzene, giving no colour in cold sulphuric acid (Found: C, 94·2; H, 5·5. $C_{23}H_{16}$ requires C, 94·5; H, 5·5%).

1-(1 : 2 : 3 : 4-*Tetrahydro*-1-*oxo*-2-*naphthylidenemethyl*)*pyrene* (IX).—Pyrene-1-aldehyde (m. p. 127°, b. p. 287°/17 mm.) was prepared by formylation of pyrene with dimethylformamide, at variance with the literature.[12] Treatment of this aldehyde (4 g.) with α-tetralone (2·5 g.) in the presence of ethanolic potassium hydroxide afforded the *product* as deep yellow leaflets (5·2 g.), m. p. 200°, from ethanol–benzene (dark violet halochromy in sulphuric acid) (Found: C, 90·1; H, 5·1. $C_{27}H_{18}O$ requires C, 90·5; H, 5·1%). Cyclodehydration of this yielded no definite hydrocarbon, the only product which could be identified being pyrene (m. p. 149°; picrate, m. p. 222°) in small amounts.

1-(1 : 2 : 3 : 4-*Tetrahydro*-1-*oxo*-2-*phenanthrylidenemethyl*)*pyrene* (X).—This *ketone* was prepared from 1 : 2 : 3 : 4-tetrahydro-1-oxophenanthrene (2·6 g.) and pyrene-1-aldehyde (3 g.) in 4% ethanolic potassium hydroxide (100 c.c.). Crystallisation from ethanol–benzene afforded deep yellow leaflets (3 g.), m. p. 258—260° (dark violet halochromy in sulphuric acid) (Found: C, 91·0; H, 4·6. $C_{31}H_{20}O$ requires C, 91·2; H, 4·9%). The isomeric 1-(1 : 2 : 3 : 4-*tetrahydro*-4-*oxo*-3-*phenanthrylidenemethyl*)*pyrene* (XI), prepared similarly, crystallised as yellow prisms, m. p. 220° from ethanol–benzene (violet halochromy in sulphuric acid) (Found: C, 90·9; H, 5·0%). Attempts to cyclodehydrate these ketones resulted only in the separation of some pyrene.

2′-*Benzylidene*-1′ : 2′ : 3′ : 4′-*tetrahydro*-1′-*oxo*-1 : 2-*benzopyrene* (XII).—1′ : 2′ : 3′ : 4′-Tetrahydro-4′-oxo-3 : 4-benzopyrene (m. p. 178°) was prepared from pyrene and succinic anhydride as described,[13] except that the keto-acid was reduced by hydrazine hydrate and potassium hydroxide. Condensation of it (3 g.) with benzaldehyde (1·2 g.) furnished the *ketone* (XII) which formed yellow needles (3·2 g.), m. p. 194°, from ethanol–benzene (violet-red halochromy in sulphuric acid) (Found: C, 90·8; H, 5·1%).

Fluoreno(3′ : 4′-1 : 2)*pyrene* (XIII).—Cyclodehydration of the foregoing ketone (3 g.) with phosphoric oxide (2 g.) afforded a *hydrocarbon*, crystallising as yellow leaflets (0·8 g.), m. p. 235°, from ethanol–benzene (Found: C, 95·0; H, 4·9. $C_{27}H_{16}$ requires C, 95·3; H, 4·7%).

1′ : 2′ : 3′ : 4′-*Tetrahydro*-2′-(1-*naphthylmethylene*)-3′-*oxo*-1 : 2-*benzopyrene* (XIV).—This *ketone*, prepared as above from 1-naphthaldehyde, formed deep yellow needles, m. p. 235°, from benzene (deep violet halochromy in sulphuric acid) (Found: C, 90·9; H, 5·0%).

7′ : 8′-*Benzofluoreno*(3′ : 4′-1 : 2)*pyrene* (XV).—Cyclodehydration of the foregoing ketone (2 g.) yielded, on distillation *in vacuo*, a portion, b. p. >300°/1 mm., which on crystallisation from *cyclo*hexane, gave the *hydrocarbon* as golden leaflets (0·7 g.), m. p. 286—287° (decomp. >250° if heated in the air) (violet halochromy in sulphuric acid) (Found: C, 95·1; H, 4·4. $C_{31}H_{18}$ requires C, 95·4; H, 4·6%).

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THE RADIUM INSTITUTE, THE UNIVERSITY OF PARIS. [*Received, July 30th*, 1957.]

[12] Vollmann, Becker, Corell, and Streeck, *Annalen*, 1937, **531**, 35.
[13] Cook, Hewett, and Hieger, *J.*, 1933, 395.

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11. *Vibrational Frequencies of Substituted Ammonium Ions.*

By P. J. Stone, J. Cymerman Craig, and H. W. Thompson.

The infrared spectra of some solid secondary and tertiary amine hydrohalides have been measured. Characteristic stretching and deformation vibration frequencies of NH_2^+ and NH^+ have been derived, and the assignments have been substantiated by measurements on the deuterated compounds.

Although much is known about the vibrations of NH_2 and NH groups in primary and and secondary amines, the characteristic vibration frequencies of the substituted ammonium ions $-NH_3^+$, $>NH_2^+$, and $\geqslant NH^+$ in the amine hydrohalides are still uncertain. Earlier evidence from the infrared absorption spectra was reviewed by Bellamy,[1] by Witkop,[2] and more recently by Heacock and Marion.[3] The last authors measured the spectra of several secondary amine hydrochlorides and derived a value close to 1600 cm.$^{-1}$ for a deformational vibration frequency of the NH_2^+ group.

We have measured the infrared spectra of some solid secondary and tertiary amine hydrohalides, both in potassium chloride discs and in mulls of Nujol and Fluorolube, in order both to assign the characteristic vibration frequencies and also to study the band intensities, since other work on the intensities of NH group vibrations in different secondary amines has revealed interesting correlations with structure.[4] While it has proved impracticable to obtain satisfactory intensity data in these cases owing to difficulties with the disc method and also because of the highly hygroscopic nature of some of the compounds, some new frequency assignments have been deduced which are substantiated by spectral comparisons with the deuterated materials. The greater dispersion which we have used in the region 3—4 μ has also enabled us to disentangle the complex situation arising from the overlapping of the stretching vibration bands of the C–H and N^+–H bonds.

Experimental

The spectra were measured over the range 600—4000 cm.$^{-1}$ on a Perkin-Elmer 21 spectrometer with a rock-salt prisms, and the region 2000—3000 cm.$^{-1}$ was examined further under higher dispersion with a Perkin-Elmer 12 C instrument fitted with a lithium fluoride prism. The potassium chloride used for making the pressed discs was repurified by precipitation from a saturated aqueous solution with hydrochloric acid. It was heated *in vacuo* at about 450° for several days to remove residual water. Additional care was necessary to prevent further adsorption of water vapour by the amine hydrohalides themselves. This adsorbed water was revealed especially by its broad absorption near 3 μ, and it was extremely difficult to obtain records entirely free from it. However, if adequate precautions were taken, the spectral records of the solids in potassium chloride discs were essentially identical with those obtained by using mulls in Nujol or Fluorolube.

The compounds were specially prepared and the following recorded m. p.s indicated satisfactory purity: diethylamine hydrochloride 223·5°, dibenzylamine hydrochloride 255—256°, piperidine hydrochloride 242°, piperazine dihydrochloride 322—323°, morpholine hydrochloride 175—176°, thiazine hydriodide 156—157°, *N*-methylpiperidine hydriodide 121·5°, *N*-benzylpiperidine hydrochloride 176—178°, benzyldimethylamine hydrochloride 173—174°, *N*-ethylmorpholine hydriodide 147—148°, *N*-benzylmorpholine hydrochloride 243—244°, *N*-benzyl-*N'*-methylpiperazine dihydrochloride 257—258°, *N*-benzylpiperazine hydrochloride 167·5—168°.

Deuteration was carried out as follows. The amine hydrohalide was placed in a small glass tube attached to a vacuum line, and adsorbed water was removed by prolonged evacuation. Dry air was then admitted to the line, and 99% deuterium oxide added to the solid from a

[1] Bellamy, "The Infra-red Spectra of Complex Molecules," Methuen, London, 1954.
[2] Witkop, *Experientia*, 1954, **10**, 420.
[3] Heacock and Marion, *Canad. J. Chem.*, 1956, **34**, 1782.
[4] Russell and Thompson, *J.*, 1955, 483; *Proc. Roy. Soc.*, 1956, *A*, **234**, 318.

dropping funnel sealed to the apparatus. After an interval, the heavy water was pumped off; this process was repeated several times. A high degree of deuteration was thus achieved and, although it was incomplete, the marked changes of intensity of certain bands could be used as a guide to the assignments.

Results

In the spectra of the secondary amine hydrohalides there are two regions of particular interest. One includes a complex pattern of bands between 2500 and 3000 cm.$^{-1}$, and the other lies between 600 cm.$^{-1}$ and 1600 cm.$^{-1}$. The former includes the stretching vibrations of the substituted ammonium ion, and the latter its deformational modes in addition to vibrations of the whole skeleton. After deuteration, a new group of bands appears between 1900 cm.$^{-1}$ and 2300 cm.$^{-1}$, in which the N^+–D stretching vibration bands are present, and there are other new bands around 1100 cm.$^{-1}$ and at lower frequencies. Simultaneously with the appearance of these new bands there are changes in the spectra near 3000 cm.$^{-1}$ and 1600 cm.$^{-1}$ as compared with those of the undeuterated compounds. Both before and after deuteration the spectra are very complex, with many of the strongest bands appearing to consist of several components, and it is quite impossible to make many direct assignments of vibration frequencies. There appear to be many combination or difference bands which cannot yet be interpreted. The situation is complicated further by the possibility of hydrogen-bond formation, some of which may arise from the presence of residual water in the solids. However, the results obtained upon deuteration lead to a few definite assignments.

First, with the secondary amine hydrohalides containing the $>NH_2^+$ ion, there are two N–H stretching vibration bands, the symmetric and antisymmetric vibrations, at about 2800 cm.$^{-1}$ and 2920 cm.$^{-1}$ respectively, which decrease in intensity upon deuteration. Two new bands then appear, near 2120 cm.$^{-1}$ and 2200 cm.$^{-1}$. The results are given in Table 1, and the positions quoted for the bands should be regarded as correct to within 10 cm.$^{-1}$, but cannot be fixed more precisely because of their broad nature and overlap with other bands. In the case of piperazine dihydrochloride the assignments are doubtful, owing to an unusual complexity which was also noted by Heacock and Marion.[3]

Table 1. $>NH_2^+$ *stretching vibrations.*

	Asymmetric			Symmetric		
	ν(H)	ν(D)	Ratio	ν(H)	ν(D)	Ratio
Diethylamine hydrochloride	2915	2195	1·33	2824	2100	1·34
Dibenzylamine ,, ...	2920	2212	1·32	2789	2112	1·32
Piperidine ,, ...	2920	2170	1·35	2844	2117	1·35
Morpholine ,, ...	2920	2220	1·32	2780	2108	1·32
Thiazine hydriodide	2920	2223	1·32	2820	2164	1·30
Piperazine dihydrochloride	2950?	2281?	(1·29)	2840?	2093	(1·36)

Table 1 includes the frequency ratios for the isotopic species. If the N^+–H link is regarded as the vibrating molecule, the ratio should be close to 1·37, and Edsall [5] found values of about 1·36 for the vibrational frequencies of the NH_3^+ ion from Raman spectral measurements on methylamine and hydrazine hydrochlorides. The ratios now observed therefore support the assignments suggested.

Near 1600 cm.$^{-1}$ there is another sharp band of the secondary amine hydrohalides which is replaced by another around 1200 cm.$^{-1}$ after deuteration. The results are given in Table 2. This band is clearly due to a deformational mode of the ion and supports the assignments made by Heacock and Marion. Indeed, the band of amino-acid hydrochlorides in this region discovered earlier by Randall *et al.*[6] can now be definitely associated with the $>NH_2^+$ group deformation. The new point to note is that its exact location

[5] Edsall, *J. Chem. Phys.*, 1940, **8**, 520.
[6] Randall, Fowler, Fuson, and Dangl, "Infra-red Determination of Organic Structures," van Nostrand, New York, 1949.

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depends upon the particular residues attached to this group. There is in fact a rough correspondence between the value of this frequency and the σ^* values of the attached groups, discussed by Taft.[7] As σ^* increases, the frequency is lowered. Thus with the

TABLE 2. $>NH_2^+$ *Deformational mode.*

	ν(H)	ν(D)	Ratio
Diethylamine hydrochloride	1600	1178	1·36
Dibenzylamine ,,	1572	1160	1·36
Piperidine ,,	1598	1240	1·29
Morpholine ,,	1580	1275	1·24
Thiazine hydriodide	1560	1140	1·37
Piperazine dihydrochloride	1591	—	—
N-Benzylpiperidine hydrochloride	1597	—	—

hydrochlorides of *N*-phenylglycine, diphenylamine, dibenzylamine, *N*-ethylaniline, dimethylamine, and diethylamine, for which $\sigma^* = 1{\cdot}65$ 1·20, 0·45, 0·50, 0, and −0·2, the frequencies are 1560, 1572, 1572, 1589, 1600, and 1600 cm.$^{-1}$ respectively.

In the spectra of the secondary amine hydrohalides there are two other prominent bands near 2500 cm.$^{-1}$ and 2400 cm.$^{-1}$, which decrease in intensity after deuteration. These must be connected in some way with the $>NH_2^+$ group, and as Table 3 shows there is a regular relation between these bands and those assigned above to the stretching vibrations of this group. The interpretation of this pair of bands is uncertain. They could arise as difference bands caused by absorption from a low-frequency fundamental near 400 cm.$^{-1}$, or alternatively as vibrations of the $>NH_2^+$ group lowered by hydrogen bonding either with other similar groups or even with residual water in the solid.

TABLE 3.

	ν_a	ν_{sym}	Δ	ν_b	$\nu_{antisym}$	Δ
Diethylamine hydrochloride	2390	2824	434	2483	2915	432
Piperidine ,,	2427	2844	417	2496	2920	434
Morpholine ,,	2461	2780	329	2605	2920	315
Thiazine hydriodide	2400	2820	420	2484	2920	436
Piperazine dihydrochloride	2426	2840	424	2515	2950	435

With the tertiary amine hydrohalides, an assignment of the $>NH^+$ group stretching vibration has been made as given in Table 4. The frequency ratio for the isotopic species is between 1·25 and 1·30. These results agree with earlier suggestions by Lord and Merrifield [8] for triethylamine hydrochloride and pyridine hydrochloride, also included in Table 4.

TABLE 4. $>NH^+$ *Stretching vibration.*

	ν(H)	ν(D)	Ratio
N-Methylpiperidine hydrochloride	*ca.* 2680	*ca.* 2068	1·30
N-Ethyl morpholine ,,	2665	2046	1·30
Benzyldimethylamine ,,	2630	2023	1·30
N-Benzylpiperidine ,,	2512	1962	1·28
N-Benzylmorpholine ,,	2480	1980	1·25
N-Benzyl-*N'*-methylpiperazine dihydrochloride	2330	1850	1·26
Triethylamine hydrochloride	2540	1965	1·29
Pyridine ,,	2425	1880	1·29

This work was supported by a grant from the Hydrocarbon Research Group of the Institute of Petroleum, whom we thank.

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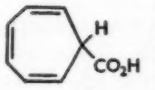
[7] See Newman, " Steric Effects in Organic Chemistry," Wiley, New York, 1956.
[8] Lord and Merrifield, *J. Chem. Phys.*, 1953, **21**, 166.

12. *The Tropylium Ion. Part III.*[1] *Oxidation of* cyclo*Hepta-2 : 4 : 6-trienecarboxylic Acid.*

By M. J. S. Dewar, C. R. Ganellin, and R. Pettit.

Oxidation of *cyclo*hepta-2 : 4 : 6-trienecarboxylic acid by several agents is found to give tropylium salts. The other main product is terephthalic acid. The mechanism of these reactions is discussed.

Oxidation of the tropylium cation by acidic permanganate to benzaldehyde, reported in Part I [1] of this series, has since been of some use for the detection of tropylium salts in dilute aqueous solutions. However, it was later found that the test is of limited application, for *cyclo*hepta-2 : 4 : 6-trienecarboxylic acid * (I), which is the starting material in the synthesis of the tropylium cation described in Part I, is also oxidised to benzaldehyde under these conditions. This led us to investigate further the oxidation of the acid (I), for from the above experiments the most likely mechanism for the formation of benzaldehyde seemed to involve intermediate formation of the tropylium cation.



(I)

Buchner [3] first investigated the oxidation of *cyclo*hepta-2 : 4 : 6-trienecarboxylic acid, obtaining a variety of products depending on the conditions used. Thus, oxidation with acidic permanganate gave benzaldehyde, benzoic acid, terephthalic acid, phthalic acid, and *trans-cyclo*propane-1 : 2 : 3-tricarboxylic acid, accounting together for about 10% of the starting material.

We have repeated the oxidation with acidic permanganate and, under suitable conditions, have obtained yields of up to 40% of tropylium salts, together with some of Buchner's products. Tropylium salts were isolated from the aqueous reaction mixture by conversion into ditropyl ether, which was extracted and converted by hydrogen bromide into tropylium bromide. Buchner had presumably also obtained solutions of tropylium salts but since these compound have unusual properties and were then unknown their presence could hardly have been suspected.

The other products isolated in the present instance were benzaldehyde and benzoic acid.

We have also studied the reaction of *cyclo*hepta-2 : 4 : 6-trienecarboxylic acid with a number of other oxidising agents, with the results tabulated. These suggest that two types of oxidation take place. Benzaldehyde and benzoic acid are known to be formed on oxidation of tropylium salts, and in these cases tropylium is probably the primary product;

Oxidant	Products	Oxidant	Products
Acidic $KMnO_4$	Tropylium salts, Ph·CHO, $Ph·CH_2·CO_2H$	Alkaline H_2O_2	α-*cyclo*Heptatrienecarboxylic acid
Neutral $KMnO_4$	Ph·CHO	Acid H_2O_2	No reaction
Alkaline $KMnO_4$	p-$C_6H_4(CO_2H)_2$	HNO_3	BzOH, p-$C_6H_4(CO_2H)_2$
$Pb(OAc)_4$	Tropylium salts	HIO_4	Tropylium salts, BzOH, Ph·CHO, p-$C_6H_4(CO_2H)_2$
$Na_2S_2O_8$	Tropylium salts, p-$C_6H_4(CO_2H)_2$		
$(NH_4)_2Ce(NO_3)_6$	Tropylium salts	CrO_3	p-$C_6H_4(CO_2H)_2$

indeed tropylium salts have been isolated in 20—40% yield from the reactions of *cyclo*hepta-2 : 4 : 6-trienecarboxylic acid with acidic permanganate, ceric ammonium nitrate, or lead tetra-acetate. The formation of terephthalic acid must, however, involve a different mechanism.

The formation of tropylium ions presumably involves an overall two-electron oxidation of the type outlined by Levitt.[4] Reactions of this kind are well known in the oxidation of acids $R·CO_2H$ when R^+ is a stable ion, *i.e.*, $R·CO_2H \longrightarrow R^+ + CO_2H^+ + 2e$;

* In Part I [1] we referred to norcaradienecarboxylic acid; recent work [2] has shown that a *cyclo*hepta-2 : 4 : 6-triene formulation (I) for this compound is more reasonable than the bicyclic structure.

[1] Parts I and II, *J.*, 1956, 2021, 2026.
[2] Doering, Laber, Vorderwahl, Chamberlain, and William, *J. Amer. Chem. Soc.*, 1956, **78**, 5448.
[3] Buchner, *Ber.*, 1896, **29**, 106; Braren and Buchner, *Ber.*, 1901, **34**, 995.
[4] Levitt, *J. Org. Chem.*, 1955, **20**, 1297.

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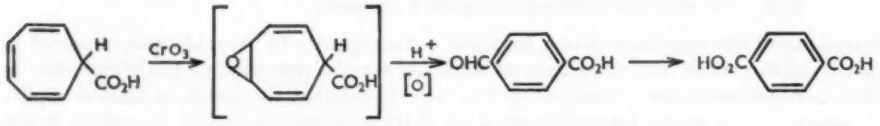
for example, α-amino-acids, $R'\cdot CH(NH_2)\cdot CO_2H$, are oxidised to aldehydes *via* the ion $R'\cdot CH{:}NH_2^+$, and triphenylacetic acid to triphenylmethanol *via* the ion Ph_3C^+. The electrons may of course be removed successively, and ionisation of the acid may precede oxidation.

The formation of terephthalic acid probably involves attack on the 4 : 5-bond of *cyclo*heptatrienecarboxylic acid, followed by a Wagner–Meerwein rearrangement, *e.g.*:



Hickinbottom and his collaborators [5] have shown that chromic acid oxidation of olefins takes place by preliminary oxidation of the C=C bond to give an epoxide, and epoxides readily rearrange in acid. It is interesting that terephthalic acid was the sole product isolated on reaction with chromium trioxide; chromium trioxide seems invariably to oxidise by hydrogen abstraction or oxygen-donation rather than by electron-transfer. It is also interesting that Buchner, using acid permanganate, isolated phthalic acid; this could have been formed by an analogous attack on the 2 : 3-bond. *iso*Phthalic acid, on the other hand, has never been obtained by oxidation of the acid (I), in accord with formulation of the acid as a *cyclo*heptatriene derivative rather than a norcaradiene derivative (when the double bonds would be in the 3 : 4- and the 5 : 6-positions).

Of the two remaining oxidation products given in the Table, phenylacetic acid was obtained only in small amounts and was probably present as an impurity in the *cyclo*hepta-2 : 4 : 6-trienecarboxylic acid, arising by substitution of ethyl diazoacetate into benzene; the other, α-*cyclo*heptatrienecarboxylic acid, was obtained only with alkaline hydrogen peroxide, and alkali is known to isomerise the acid (I) to the α-isomer. Buchner also isolated *trans-cyclo*propane-1 : 2 : 3-tricarboxylic acid in very small amounts from the products given by acidic permanganate. We have not isolated this product and it is probable that it was present as an impurity, arising by self-addition of the decomposition products of ethyl diazoacetate. It is significant that the *cyclo*hepta-2 : 4 : 6-triene-carboxylic acid described by Buchner melted below 0°, while the pure acid melts at 25°.

Experimental

cyclo*Hepta*-2 : 4 : 6-*trienecarboxylic Acid*.—Ethyl *cyclo*hepta-2 : 4 : 6-trienecarboxylate, was prepared [1] from ethyl diazoacetate and benzene, was distilled and then fractionated through a column packed with Dixon gauzes and surrounded by a heating jacket, giving pure ester, b. p. 51—53°/0·1 mm., $n_D^{22\cdot5}$ 1·5008 (impurities decrease n).

The ester was hydrolysed [1] in acetone–sulphuric acid and the product fractionated through a column packed with glass helices to give pure *cyclo*hepta-2 : 4 : 6-trienecarboxylic acid, b. p. 103—105°/0·4 mm., n_D^{18} 1·5400 (impurites increase n), solidifying to needles, m. p. 24°, $\lambda_{min.}$ 2235 (log ε 2·98), $\lambda_{max.}$ 2580 Å (log ε 3·54).

Oxidation with Potassium Permanganate.—(*a*) To the trienecarboxylic acid (15·0 g., 0·11 mole), acetone (70 ml.), and 4N-sulphuric acid (20 ml.), stirred at 0°, was added potassium permanganate (18 g., 0·11 mole) in 2N-sulphuric acid (300 ml.) in a continuous stream (10 min.); the temperature rose to 35° and stirring was continued until the mixture became clear. The mixture was cooled and extracted with ether (4 × 100 ml.). The combined extracts were washed with water, alkali (twice), and water, and dried (Na_2SO_4). Removal of the solvent gave oily neutral products (0·32 g.). The combined alkali-washings were acidified and extracted with ether (4 × 100 ml.). The last ether extracts were washed with water and dried (Na_2SO_4). Removal of the solvent gave the acidic products (1·58 g.). The original reaction mixture was made alkaline with sodium hydroxide and extracted with ether (4 × 200 ml.). These ether extracts were washed with water and dried (Na_2SO_4). Removal of the solvent gave ditropyl ether (4·10 g., 38%).

[5] Hickinbottom, Peters, and Wood, *J.*, 1955, 1360.

The mixture of neutral products gave an impure 2 : 4-dinitrophenylhydrazone which was chromatographed with benzene on alumina. Evaporation of the eluant gave benzaldehyde 2 : 4-dinitrophenylhydrazone (0·15 g., 1%), orange needles (from ethyl acetate), m. p. 235—236°, mixed m. p. 236—237°.

Trituration of the acid products with ether gave an unidentified *solid* which was filtered off (0·02 g.) and purified by vacuum sublimation (m. p. 229—229·5°) (Found: C, 67·3; H, 5·6. $C_{10}H_{10}O_3$ requires C, 67·4; H, 5·7%). The ethereal filtrate was evaporated and the residue extracted several times with warm light petroleum (b. p. 40—60°); partial evaporation of the petroleum extract gave phenylacetic acid (0·25 g., 1½%) which, recrystallised from light petroleum, had m. p. 75—77°, mixed m. p. 76—77°. The petroleum filtrate was evaporated to leave *cyclo*hepta-2 : 4 : 6-trienecarboxylic acid (0·30 g., 2%).

The ditropyl ether was purified by vacuum-distillation, then having b. p. 98—100°/0·6 mm., n_D^{17} 1·5778. The distillate was initially colourless but in a few minutes became pale yellow. Ditropyl ether (0·500 g.) was treated in dry ether (30 ml.) with a saturated solution of hydrogen bromide in dry ether. The precipitate of tropylium bromide was filtered off (0·842 g., 98%), washed with dry ether, and crystallised from absolute ethanol [m. p. 199° (decomp.)]. With aqueous picric acid solution, tropylium picrate was formed, having m. p. 97—99° (decomp.); several recrystallisations from water containing picric acid did not change this m. p. (Found: C, 40·3; H, 2·7; N, 15·0. Calc. for $C_{19}H_{14}O_{15}N_6$: C, 40·3; H, 2·5; N, 14·9%).

(*b*) When a similar ratio of permanganate to *cyclo*hepta-2 : 4 : 6-trienecarboxylic acid was used under alkaline conditions at room temperature much starting material was recovered. The only product isolated was terephthalic acid (5%) [dimethyl ester, m. p. 137—139°, mixed m. p. 138—140° (Found: C, 61·8; H, 5·3. Calc. for $C_{10}H_{10}O_4$: C, 61·8; H, 5·2%)].

(*c*) When a larger proportion of permanganate to *cyclo*hepta-2 : 4 : 6-trienecarboxylic acid was used, benzoic acid was also isolated (m. p. and mixed m. p. 120—121°).

Oxidation with Lead Tetra-acetate.—To a stirred solution of *cyclo*hepta-2 : 4 : 6-trienecarboxylic acid (1·0 g., 0·0074 mole) in acetic acid (10 ml.) at 70° was added in 5 min. a suspension of lead tetra-acetate (4·0 g., 0·0091 mole) in acetic acid (10 ml.). The mixture was poured into water (100 ml.) containing 2N-nitric acid (10 ml.), and washed with ether (3 × 50 ml.), made alkaline with sodium hydroxide, and extracted again with ether (3 × 50 ml.). The last ether extracts were washed with water, dried (Na_2SO_4), and evaporated, and the residue dried in a vacuum, taken up in dry ether (20 ml.), and treated with hydrogen bromide. The resulting precipitate of tropylium bromide was collected (0·25 g., 20%). No other product was identified.

Oxidation with Ceric Ammonium Nitrate.—A solution of ceric ammonium nitrate (9·0 g., 0·016 mole) in 2N-nitric acid (60 ml.) was added with stirring to one of *cyclo*hepta-2 : 4 : 6-trienecarboxylic acid (1·0 g., 0·0074 mole) in acetone (20 ml.) at room temperature. The mixture was washed with ether (3 × 50 ml.), made alkaline as above, and extracted again with ether (4 × 100 ml.). From the last ether extracts tropylium bromide (0·37 g., 30%) was obtained as described above. No other product was identified.

Oxidation with Persulphate.—To a stirred suspension of *cyclo*hepta-2 : 4 : 6-trienecarboxylic acid (1·0 g., 0·0074 mole), in 4N-sulphuric acid (20 ml.) containing a catalytic amount of silver nitrate at 70°, was added in 10 min. an aqueous solution of sodium persulphate (1·8 g., 0·0076 mole). The mixture was extracted with ether (3 × 50 ml.) from which terephthalic acid (0·05 g., 4%) was isolated. The aqueous mixture was then made alkaline and extracted with ether (4 × 100 ml.), whence tropylium compounds were isolated as the picrate (0·17 g., 7·2%) by conversion into the bromide and addition of aqueous picric acid.

Oxidation with Periodic Acid.—An aqueous solution of periodic acid (1·4 g., 0·0073 mole) was added in 10 min. to a stirred suspension of *cyclo*hepta-2 : 4 : 6-trienecarboxylic acid (1·0 g., 0·0074 mole) in 4N-sulphuric acid (25 ml.) at 80°. The mixture was cooled and extracted with ether (3 × 50 ml.). The combined ether extracts were washed twice with alkali and evaporated, benzaldehyde being then isolated as 2 : 4-dinitrophenylhydrazone (0·05 g., 2%). The combined alkali washings were acidified and extracted with ether (3 × 50 ml.). Evaporation of these ether extracts gave benzoic (0·03 g., 3%) and terephthalic acid (0·02 g., 1½%). The residual aqueous mixture was made alkaline and extracted with ether (3 × 50 ml.), whence tropylium picrate (0·03 g., 1½%) was obtained.

Oxidation with Nitric Acid.—*cyclo*Hepta-2 : 4 : 6-trienecarboxylic acid (2·0 g.) was added to nitric acid (25 ml.; *d* 1·42) at 3°. A deep green colour developed which was destroyed as the

mixture warmed to room temperature. The mixture was finally heated on a steam-bath until the evolution of nitrogen oxides was negligible. Terephthalic acid, which separated, was filtered off (0·15 g., 6%) and identified as the dimethyl ester. The filtrate was extracted with ether, from which benzoic acid (0·07 g., 4%) was isolated. No other oxidation product was identified.

When the oxidation was repeated without warming, no oxidation products could be isolated after 20 min.

*Oxidation with Chromic Acid.—cyclo*Hepta-2 : 4 : 6-trienecarboxylic acid (2·0 g., 0·015 mole) was added to a solution of chromic acid (4·5 g., 0·045 mole) in acetic acid (50 ml.) containing 4N-sulphuric acid (5 ml.) at room temperature. The oxidant was rapidly reduced and the temperature rose to 80°. Terephthalic acid (0·10 g., 4%), identified as the dimethyl ester, was the only product isolated.

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MILE END ROAD, LONDON, E.1. [*Received, August 8th,* 1957.]

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13. *Nitrosation, Diazotisation, and Deamination. Part I. Principles, Background, and Method for the Kinetic Study of Diazotisation.*

By E. D. HUGHES, C. K. INGOLD, and J. H. RIDD.

Diazotisation will be shown to depend kinetically on a process ending in *N*-nitrosation to form a nitrosammonium ion, all subsequent steps being fast; and the process leading to nitrosation may consist of several steps, and take a number of alternative courses, depending on the nitrosation carrier. Nitrosation carriers are considered in relation to the kinetics to which they should give rise, and it is seen that there is not a one-to-one correlation. The result is that we have to demonstrate a variety of kinetic forms, and trace transitions between them, before any certainty can be attained as to the carriers.

The earlier history of diazotisation kinetics contains many apparent disagreements which require reconciliation.

The conditions to be satisfied in an experimental kinetic investigation are considered. It is emphasised that, in a reaction between members of Brönsted acid–base systems, a clear distinction must be kept between stoicheiometric and molecular rate-constants.

THE general study indicated in the serial title is here begun with a group of papers on the kinetics of the diazotisation of aromatic amines. This paper deals with the approach, the next four record experimental results, whilst in the last of the set a collective discussion is given.

The approach has three aspects, that of general theoretical principles, that of known results and conclusions, and that of the basically known, but now refined, experimental method, and the computational procedure.

(1) THE CONDITIONS GOVERNING DEDUCTION OF MECHANISM FROM OBSERVED KINETICS OF DIAZOTISATION

(a) *Outline Mechanism.*—It will shorten discussion partly to anticipate conclusions by stating at once that results will be interpreted on the basis that diazotisation is rate-controlled by the formation of a primary nitrosamine, and that, accordingly, the investigation is one of *N*-nitrosation of primary aromatic amines, and so is valid as a contribution to the kinetics of nitrosation generally:

$$Ar{\cdot}NH_2 \xrightarrow{\text{Slow}} Ar{\cdot}NH{\cdot}NO \xrightarrow{\text{Fast}} Ar{\cdot}N{:}N{\cdot}OH \xrightarrow{\text{Fast}} Ar{\cdot}N{:}N^+ + OH^- \quad . \; . \; (1)$$

Evidence that the reaction goes through the nitrosamine comes first from the behaviour of secondary amines: here, a prototropic change cannot occur, and hence the reaction stops at the nitrosamine stage. According to Hantzsch,[1] primary aromatic nitrosamines pass into diazonium ions in aqueous acid. The assumed high rate of prototropic change is consistent with all that is known of the speed of protolysis from nitrogen and oxygen. Further, the consistency of the kinetic picture now to be described itself shows that transformations of the primary nitrosation product do not affect the kinetics of diazotisation.

Nitrosation is an electrophilic substitution, and hence must consist in the binding, by externally disposed electrons, usually atomic $2p$- or molecular 2π-electrons, of the entity NO^+, furnished either in the free form, or in a carrier NOX from which the binding p- or π-electrons can extract the NO portion. This implies that, supposing the nitrosating agent to have been supplied, the first step of diazotisation is attack of the latter on the lone-pair electrons of the primary amine. That is to say, the formation of the nitrosamine must itself involve two steps, of which the second, as a protolysis from nitrogen, is assumed to be rapid:

$$Ar{\cdot}NH_2 \xrightarrow{\text{Slow}} Ar{\cdot}NH_2{\cdot}NO^+ \xrightarrow{\text{Fast}} Ar{\cdot}NH{\cdot}NO \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

(b) *The Reactants.*—It is implied in section (1a) that the aromatic amine is attacked in its molecular, basic form, not as its ammonium ion. This was suggested by Bamberger [2] and again, with reasoned support, by Hammett,[3] though expressions of the opposite idea, notwithstanding that it is contrary to the long-established classification of polar reagents, were much more frequently seen up to 1950. Although specific proof that the free base is attacked is supererogatory in the light of modern theory, such proof is contained in the kinetic pattern to be disclosed, the consistency of which requires this conclusion.

As to carriers, nitrosation is expected to resemble other electrophilic substitutions, such as nitration and chlorination, in having a family of them: quite generally in electrophilic substitution a carrier is the introduced group, electron-depleted, and thereafter combined either with nothing or with a molecular or anionic base of any basicity up to that of the lyate ion. We shall refer to the following actual or possible carriers in nitrosation.

$$NO^+,\ NO{\cdot}OH_2^+,\ NO{\cdot}Hal,\ NO{\cdot}NO_2,\ NO{\cdot}NO_3,\ NO{\cdot}OAc,\ NO{\cdot}OH \quad . \quad . \quad . \quad . \quad . \quad (3)$$

They are here arranged in order of increasing basic strength of the combined base, that is, decreasing the electrophilic reactivity of the carrier. But the relative practical value of different carriers in given conditions depends, not only on their specific activities, but also on concentration limits governed by their thermodynamic stabilities. The generally opposed variation of these two factors from case to case leads to a certain spread of nitrosating value among the different carriers. It is thus a task in experimental kinetics to identify them in operation. The distinction required is not an elementary one, as if each carrier produced a distinct form of kinetics. To identify a carrier it is usually necessary to establish at least two kinetic forms, and particularly to demonstrate a transition between them, as in the recognition of the nitronium ion NO_2^+, and the chlorinium ion Cl^+, in nitration and chlorination, respectively. Our anticipation of this situation governs the kinetic approach to the mechanism of diazotisation.

We start with a maximally simplified nitrosating system, one from which all carrier-forming anions, such as halide, nitrate, carboxylate ions, etc., that can be excluded, have been. Since nitrosonium perchlorate does not exist in molecular form, a dilute aqueous solution of sodium nitrite and perchloric acid satisfies the required conditions. Our list of possible carriers is now reduced to the following:

$$NO^+,\ NO{\cdot}OH_2^+,\ NO{\cdot}NO_2,\ NO{\cdot}OH \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

[1] Cf. Saunders, "The Aromatic Diazo-compounds," Edward Arnold and Co., London, 1949, p. 134.
[2] Bamberger, *Ber.*, 1894, **27**, 1948.
[3] Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., New York, 1940, p. 294.

(c) *Reactants and Kinetic Form.*—We may use the abridged list (4) in order to provide a concise illustration of the type of correlation that exists between the active carrier and the kinetic form of reaction. With a general carrier, two limiting kinetic forms can be found (and one of these may have alternatives), according as the attack or formation of the carrier is rate-controlling. In the former case, the carrier remains in equilibrium with other nitrous species, and the concentration of carrier thus determined has to be multiplied by the concentration of the attacked amine in the rate-equation. In the latter case, the carrier is consumed by the amine as fast as the carrier is produced, and so the concentration of amine does not appear in the rate-equation: what is measured now is the rate of a purely inorganic process, and we have to consider the required kinetics of this, or, if there is more than one conceivable process for producing the carrier, of all of them.

The resulting kinetic equations are listed below. With molecular nitrous acid as carrier (to take the simplest of the four examples first), one kinetic case disappears, since there can be no question here of carrier-supply being rate-controlling. Only the attack of this carrier could be rate-controlling, and then the kinetic equation is (5). Similarly, the supply of nitrous acidium ion, as the first conjugate acid of nitrous acid, formed in pre-equilibrium, could not be rate-controlling. Its attack might be, and since its equilibrium concentration is determined by nitrous acid and hydrogen ion, the kinetic equation is (6). Here it may be noted that the expressions " amine " and " HNO_2 " in our kinetic equations are to be taken literally: the represented concentrations are of non-ionised molecules, not including ionic forms, which would be included in expressions of stoicheiometric concentration. Solvation is not expressed, and hence the hydrogen ion is written H^+.

Dinitrogen trioxide is a carrier of which either the attack or the formation could conceivably be rate-controlling. In the former case, an equilibrium concentration of carrier, controlled by the thermodynamics of the process, $2HNO_2 \rightleftharpoons N_2O_3 + H_2O$, will be maintained; and this concentration will be available for the attack of the amine: hence the kinetic equation is (7). In the latter case, the amine concentration drops out from the rate equation, which now represents the rate of self-dehydration of nitrous acid: this is equation (8). The nitrosonium ion also presents alternatives. If an equilibrium concentration is maintained by the thermodynamic situation, $H^+ + HNO_2 \rightleftharpoons NO^+ + H_2O$, the attack of the nitrosonium ion being rate-controlling, the kinetic equation will be (9). If the formation of nitrosonium ion is rate-controlling, and it is formed by loss of water from the nitrous acidium ion, the equation will be (10). But if formation is rate-controlling, and is by loss of nitrite ion from nitrous anhydride, the equation will be (11):

HNO_2	slow attack	Rate $\propto$ [amine][HNO_2] . . .	(5)
$H_2NO_2^+$	,, attack	,, $\propto$ [amine][HNO_2][H^+] . .	(6)
N_2O_3	,, attack	,, $\propto$ [amine][HNO_2]^2 . . .	(7)
	,, supply	,, $\propto$ [HNO_2]^2	(8)
NO^+	,, attack	,, $\propto$ [amine][HNO_2][H^+] . .	(9)
	,, supply *via* $H_2NO_2^+$	,, $\propto$ [HNO_2][H^+]	(10)
	,, supply *via* N_2O_3	,, $\propto$ [HNO_2]^2	(11)

The duplication of equations here seen is sufficient to show that one cannot expect to " locate " oneself in the total pattern without experimentally disclosing a larger part of it than would appear through the observation of just one kinetic form. Indeed, at the outset, before one has convinced oneself that none but the first steps of schemes (1) and (2) affects the kinetics, a number of additional equations, some the same as, and some different from, those here written down, have to be thought of, which allow for slow proton-transfers in the succeeding steps, *i.e.*, for general acid and general base catalysis by various nitrous species, not excluding nitrite ion as a general base. For this reason

also, a kinetic investigation is not expected to lead to proved conclusions unless it demonstrates, and elucidates, a certain kinetic variety.

The scheme represented by equations (5)—(11) is more limited than the total scheme of theoretical considerations required, and actually applied, in this work, in the following additional respect. The given set of equations applies to the abridged list of carriers (4); and our original object was to discriminate among the carriers of this list. However, we found that, in order thoroughly to confirm one of these carriers, and to complete the identification of another, we had to admit competing carriers, outside those of the abridged list: we had to study the kinetic changes which occur when the original nitrosating system is deliberately thus complicated.

However, these elaborations will be discussed when we come to them. The object of this section has been, not to set out fully all the theoretical details which have to be envisaged for the purpose of shaping the kinetic approach, but to make clear, by illustration for a limited but central area of the total field, the general nature of the approach, and the power and limitations of the kinetic method.

(2) Previous Results and Conclusions on *N*-Nitrosation, Diazotisation, and Deamination

The pioneer work was that of Hantzsch and Schumann, who, in 1899, first studied the kinetics of diazotisation.[4] They used aqueous solutions made weakly acid (0·002M) with hydrochloric acid; and they followed the reaction by an iodometric method, using equivalent amounts of reactants. They established approximate second-order kinetics, and wrote the rate-equation thus:

$$\text{Rate} = k[\text{ArNH}_3^+][\text{HNO}_2] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (12')$$

The quantities in these brackets were representing stoicheiometric concentrations of amine and of nitrous acid, to which, at constant acidity, the concentrations of molecular amine and nitrous acid are respectively proportional. Hence the equation may be re-expressed as follows with the conventions used for the rate-equations of section 1:

$$\text{Rate} \propto [\text{amine}][\text{HNO}_2] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (12)$$

Hantzsch and Schumann also concluded, though it may be doubted if anyone believed them (then or subsequently up to 1950), that to within their experimental error all aromatic primary amines diazotise at the same rate.

Tassilly [5] introduced the colorimetric method, based on coupling, for following diazotisation, and was the first to do experiments with unequal concentrations of reactants. However, he also found that the reaction, in dilute mineral acid, was approximately of second order.

Boeseken, Brandsma, and Schoutissen [6] considered all previous work in the field to be inaccurate. They developed Tassilly's principle into a more exact procedure. They used reactants in equivalence. Their results for the diazotisation of a number of amines in dilute hydrochloric acid (0·01M) confirmed that the reaction is approximately of second order. But they failed to confirm Hantzsch and Schumann's finding that the rates for different amines are equal.

However, we are reminded of the earlier finding by Reilly and Drumm's report [7] that the three anilines, p-$NH_2 \cdot C_6H_4 \cdot [CH_2]_n \cdot NMe_3^+$ with $n = 0$, 1, 2, which must have very different basic strengths, diazotise at the same second-order rate in dilute hydrochloric acid (0·002M), the reagents again being in equivalence. Disbelief in these results was at once expressed by Boeseken and Schoutissen.[8]

[4] Hantzsch and Schumann, *Ber.*, 1899, **32**, 1691.
[5] Tassilly, *Compt. rend.*, 1913, **157**, 1148; 1914, **158**, 335, 489; *Bull. Soc. chim. France*, 1920, **27**, 19.
[6] Boeseken, Brandsma, and Schoutissen, *Proc. Acad. Sci. Amsterdam*, 1920, **23**, 249.
[7] Reilly and Drumm, *J.*, 1935, 871.
[8] Boeseken and Schoutissen, *Rec. Trav. chim.*, 1935, **54**, 956.

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It will not be overlooked that equation (12) is not fully proved, since, excepting for a few somewhat uncritical experiments by Tassilly on sulphanilic acid, the reagents were always taken in equivalence. But all workers from 1899 to 1935 agree that the overall kinetic order is second. They differ as to whether different amines diazotise at the same rate or at different rates, the former opinion arising from experiments in the lower range of acidity (near 0·002M), and the latter from experiments at a somewhat higher acidity (0·01M).

In 1936, Schmid observed kinetics of a different kind.[9] He worked in a markedly higher acidity range (of the order of 0·2M). With acidities set by added sulphuric acid, the reaction was now of third order overall, as represented by the rate-equation (13):

$$\text{Rate} \propto [\text{amine}][\text{HNO}_2]^3 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (13)$$

The use of hydrochloric or hydrobromic acid in place of sulphuric acid introduced additionally a catalysed reaction, into the details of which we need not enter now. As to the basic reaction of equation (13), Schmid made no attempt to reconcile his third-order kinetics with the second-order kinetics found by all previous workers on diazotisation: he makes no reference to the previous work.

Equation (13) was not new. It had been discovered in 1928, by T. W. J. Taylor in application to the deamination of primary aliphatic amines.[10, 11, 12] In 1929, Taylor observed it again in the simplest, and kinetically most basic, of the whole family of reactions between amines and nitrous acid, the formation of a nitrosamine from a secondary amine.[12] In his first work,[10] Taylor confirmed an early suggestion by Arndt that the same equation governed the reactions of ammonia with nitrous acid; and in this he was in turn confirmed by Abel *et al.*[13]

In the many theoretical discussions of equation (13), the simplest line taken was that of Earl and Hills, who " preferred to consider " the third kinetic order as spurious.[14] They made it clear that they preferred equation (12), which they explained by supposing that the amine adds to nitrous acid, somewhat as it might add to a carbonyl compound.

Kenner, and also Hammett, on the other hand, accepted equation (13); and they offered interpretations of it. Adamson and Kenner explained it [15] by assuming that the second step, not the first, of process (2) is slow, that the first step involves specific hydrogen-ion catalysis (the reagent therefore being the nitrous acidium ion), and that the second step involves general base catalysis (with nitrite ion as the effective base), the two catalyses between them bringing into the transition state the equivalent of the second molecule of nitrous acid. Apart from the improbability that the second step of process (2) could be slow, it has been shown by Austin [16] that deamination is not subject to general base catalysis. Finally, Hammett [3] made the suggestion, which we show to be correct, that equation (13) represents a rate-controlling attack by dinitrogen trioxide, whilst in catalyses by hydrogen halide the attack is by nitrosyl halide.

We have set down this history for two reasons. The first is that, despite its recurrent disagreements, we can show that all previously recorded work can be understood, and could be accepted as essentially correct, apart from one purely logical slip, which entered at the outset and remained undetected until we noticed it. The second is that, whilst all previous authors have turned a blind eye on one " half " or the other of the recorded facts, with the consequence that their interpretations can only have the status of patently questionable suggestions, we shall show that an interpretation is available which accommodates all known facts, and is, indeed, proved by them.

[9] Schmid, *Z. Elektrochem.*, 1936, **42**, 579; 1937, **43**, 626; Schmid and Muhr, *Ber.*, 1937, **70**, 421.
[10] T. W. J. Taylor, *J.*, 1928, 1099.
[11] *Idem*, *J.*, 1928, 1897.
[12] T. W. J. Taylor and Price, *J.*, 1929, 2052.
[13] Abel, Schmid, and Schrafranik, *Z. phys. Chem., Bodenstein Festschrift*, 1931, 510.
[14] Earl and Hills, *J.*, 1939, 1089.
[15] Adamson and Kenner, *J.*, 1934, 838; Kenner, *Chem. and Ind.*, 1941, **60**, 443, 899.
[16] Austin, Thesis, London, 1950; cf. ref. 17.

We break off the history at 1950, because it was then that we first published [17] in preliminary form the main findings of which the details are now presented. Subsequent related work will be considered in the comparative discussion of Part VI.

(3) The Measurement of Diazotisation

(a) *Side-reactions in Diazotisation.*—Diazotisation has been followed by extracting samples, and determining the diazonium-ion concentrations colorimetrically. The obtained values were subtracted from the initial (stoicheiometric) concentrations of amine and nitrous acid, in order to give the reagent concentrations at the time of sampling. This method is valid only if the side-reactions of the nitrous acid and diazonium ion can be ignored. Consideration was therefore given to these side-reactions.

Several previous kinetic studies have been made of the decomposition of solutions of nitrous acid. The reaction almost certainly involves the formation and hydrolysis of dinitrogen tetroxide, but the rate-determining stage appears to depend on the experimental conditions,[18] with the result that previous work cannot be used to estimate the extent of the decomposition under the conditions of our experiments.

Therefore a brief experimental study was undertaken of this decomposition. We started with the Griess–Ilosva method for the colorimetric determination of nitrous acid; but it has the grave disadvantage that several hours are required for the colour development. However, in some joint work with Dr. E. A. Halevi, it was possible to modify the Griess–Ilsova method, so that the colour production became almost instantaneous.[19]

It was shown that, at 0°, a 0·0001M-solution of nitrous acid decomposed at a rate of 0·5—1·0% per hour, that in a 0·001M-solution the rate was 1—2% per hour, and that in a 0·005M-solution decomposition became non-uniform, the rate falling with time. These results were obtained in 0·002M-perchloric acid, but as there is no evidence for acid catalysis, other than that arising from the conversion of nitrite ions into nitrous acid, they should hold at other acidities. When these rates are compared with diazotisation rates, it becomes clear that the decomposition of nitrous acid should not greatly affect the kinetics of diazotisation.

The two conceivably significant side-reactions of diazonium ions are their hydrolysis, and their *N*-coupling with unchanged amine to give diazoamino-compounds. The hydrolysis is a simple S_N1-reaction, kinetically of the first order, and its rate has been measured.[20] From rates at higher temperatures it can be estimated that at 0° the diazonium ion from aniline will undergo hydrolysis at a rate of about 0·3% per hour. The diazonium ions from the toluidines are expected to be of the same order of stability, and those having electronegative nuclear substituents to be more stable. This reaction, then, is not an important source of error.

The *N*-coupling reaction could introduce large errors; but it can be seen, because it leads to colour. In our conditions it makes little trouble in the diazotisation of aniline and the toluidines but, in that of amines with electronegative nuclear substituents, the solutions may become coloured, and the diazonium-ion concentration may fail to reach its theoretical value and, at late times, begin to decrease. Whenever this has been observed, the amine concentration has been reduced, or the acidity has been increased, until the diazotisation goes to completion.

(b) *Kinetic Methods.*—The aromatic amines, purchased or pure, were further purified by conventional methods. The perchloric acid and sodium nitrite were "AnalaR". The latter was of better than 99% purity, as determined by the Fischer–Steinbach

[17] Hughes, Ingold, and Ridd, *Nature*, 1950, **166**, 642.
[18] Bray, *Chem. Rev.*, 1932, **10**, 161.
[19] Bunton, Halevi, and Llewellyn, *J.*, 1952, 4916.
[20] Moelwyn-Hughes and Johnson, *Trans. Faraday Soc.*, 1940, **36**, 948.

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method,[21] and no correction was made for the difference from 100%. The R-salt had to be purified by repeated crystallisation from a hot solution of sodium chloride.

The temperature of the measurements was 0·00° ± 0·05°. Solutions of the amine in an equivalent of aqueous perchloric acid, and of perchloric acid in water, were mixed to such volume that, when, after temperature adjustment, the run was started by the addition of temperature-adjusted aqueous sodium nitrite, the volume was 100 ml. Samples of 2 or 5 ml. were withdrawn at timed intervals, and run each into 27 ml. of the coupling solution, which contained R-salt (0·01M) and borax (0·025 or 0·05M).

Colour densities were measured in well-screened cells, 0·25—4·00 cm. thick, in a Hilger Spekker photo-electric absorptiometer, with a narrow-transmission-band filter, so that Beer's law was obeyed, and a sensitive galvanometer. Calibration was obtained with a colour standard, prepared in various ways for purposes of checking, but usually, and most conveniently, by diazotising the amine in known amount, with excess of nitrous acid and a slight excess of perchloric acid, conditions under which the reaction is rapid and complete. The calibration curve, obtained by dilution of the standard, was linear.

In recording the initial conditions of runs done in excess of perchloric acid, allowance was always made for the fact that the total acid is partly neutralised, not only by the amine, but also by the sodium nitrite. It is the excess, beyond these allowances, that is cited as the acidity.

Runs in buffers, or with added catalysis, were done by obvious adaptations of the methods described.

(c) *Types of Rate-constant.*—Each of our reactants is a Brönsted acid–base system. We can therefore calculate various types of rate-constant, of which two have had their uses in this work. One, which we call a stoicheiometric rate-constant, is the proportionality constant of a rate-equation containing only stoicheiometric concentrations of the reactants, *i.e.*, for each reactant a total of the concentrations of its acidic and basic forms. The other, which we call a molecular rate-constant, is the constant of a rate-equation involving the concentrations in which the reagents are present in their uncharged molecular forms. In a constant excess of acid, or, more generally, at constant hydrogen-ion concentration, the ratio of the molecular to the stoicheiometric concentration for each reactant remains constant throughout a run. Therefore, it makes no difference to the kinetic form of the run, which type of constant we calculate; but it does make a difference to the value of the constant.

The stoicheiometric rate-constants are easily computed, inasmuch as they depend only on quantities which we ourselves measure. However, the computation of molecular rate-constants requires a knowledge also of the acidity constants of the arylammonium ion and of nitrous acid. These equilibrium constants have been measured accurately only at low ionic strengths, and they have not been well measured at the moderate ionic strengths of some of our experiments. This makes no great difficulty as regards the aryl-ammonium ion, the dissociation of which does not create or destroy charges, with the consequence that its acidity constant is insensitive to ionic strength, except at high ionic strengths. However, the acidity constant of nitrous acid must be appreciably greater at moderate than at low ionic strengths.

Our policy has therefore been to calculate stoicheiometric rate-constants whenever nothing of importance depended on what type of constant was chosen, and to calculate molecular rate-constants only when they were needed, giving the employed acidity constants, so that the data could easily be corrected should more accurate acidity constants become available. The first procedure is fully satisfactory, except when we are comparing experiments at different acidities for the purpose of determining the effect of acidity; for an acidity change could in general have two kinds of effect, which it would be necessary to distinguish. First, added acid could replace amine by ammonium ion, and nitrite ion by

[21] Fischer and Steinbach, *Z. anorg. Chem.*, 1912, **78**, 134.

nitrous acid; and if the kinetics corresponded to equation (5), (7), (8), or (11) of section (1c), that would be all that it could do. But if the kinetics corresponded to equation (6), (9), or (10), or to one of the equations, not given in section (1c), which express catalysis by hydrogen halides, then an acidity change would have a further effect, inasmuch as, in these kinetic forms, hydrogen-ion becomes a reactant. For the purpose of sorting out this mechanistically significant, second effect of acid, we have to calculate molecular rate-constants.

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14. *Nitrosation, Diazotisation, and Deamination. Part II.* Second- and Third-order Diazotisation of Aniline in Dilute Perchloric Acid.*

By E. D. HUGHES, C. K. INGOLD, and J. H. RIDD.

The overall kinetic order of the diazotisation of aniline in dilute perchloric acid falls, as the excess of acid is reduced, from 3 to near 2, and finally rises to about 2·6 as the last of the excess of acid is removed. The rise is due to easily understood but uninteresting causes, whereas the fall is mechanistically significant. It is due to a fall of order in aniline from 1 to 0, the kinetic order in nitrous acid being always 2. These kinetics account for nearly all the reaction, though signs of a small acid-catalysed component can be seen.

As noted in Part I * (section 2), the diazotisation of aniline and other aromatic amines has been found to be kinetically of second order by some previous investigators and of third order by others. No one had brought these observations together, treating the two sets with equal seriousness, as presenting a problem in reconciliation. Our first objective, on taking up the subject in 1949, was to try to verify the suggested kinetic duplexity, and, if it were confirmed, to trace the variations in experimental conditions which produce the change of kinetic form. In these experiments, aniline was employed as the amine, and the temperature was 0·0° throughout. A comparison of the conditions applying to to the previously recorded observations had suggested that the difference of kinetic result might be connected with the acidity; and we soon found that this was correct. The acid employed in common by the previous investigators had been hydrochloric acid, but, for reasons which will be clear from the preliminary theoretical considerations in Part I (section 1), we preferred, at this stage of our work, to use perchloric acid.

(1) *Two Kinetic Orders and the Transition between Them.*—An overall kinetic order, even when non-integral, can be determined by the variation in the time of half-reaction with dilution of an initial reaction mixture. The relation is

$$\log t_{\frac{1}{2}} = C - (n - 1) \log a$$

where n is the overall kinetic order, a is the initial concentration of each reactant, $t_{\frac{1}{2}}$ is the half-life of the reactants, and C is a constant. This equation has been used to determine the overall reaction order for the diazotisation of aniline in various concentrations of excess of perchloric acid. By the excess of acid is meant the excess over what is required to convert the aniline into anilinium perchlorate and to liberate nitrous acid from the supplied sodium nitrite. For each excess of acid, runs were done at various dilutions of a reaction mixture containing stoicheiometrically equivalent concentrations of aniline and nitrous acid. The results are in Table 1, and a logarithmic plot of them is shown in Fig. 1. The slopes of the graphs are values of $(1 - n)$. The resulting values of the reaction order n are plotted against the concentration of excess of acid in Fig. 2.

* Part I, preceding paper.

It appears that the overall reaction order falls from almost 3 to near 2, as the acidity is reduced from 0·050 to 0·002M; but that the order rises again to about 2·6, when the excess of acid is removed altogether. These conclusions are confirmed by examination of the behaviour of integrated, stoicheiometric, second- and third-order rate-constants, $\bar{k}_2$ and $\bar{k}_3$, calculated at successive stages of individual runs. Three contrasting illustrations are given in Table 2. Of course, this is an insensitive method of determining kinetic

FIG. 1. *Diazotisation of aniline: logarithmic plot of reactant half-life* versus *reactant concentration, at various concentrations of excess of perchloric acid. (The figures are the millimolarities of the excess of acid in the several sets of experiments.)*

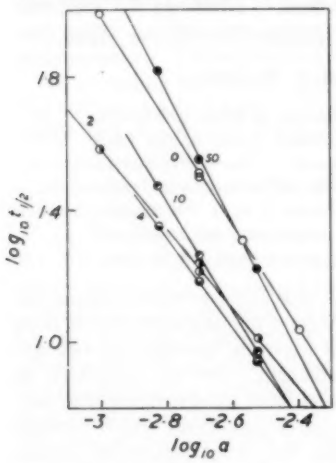
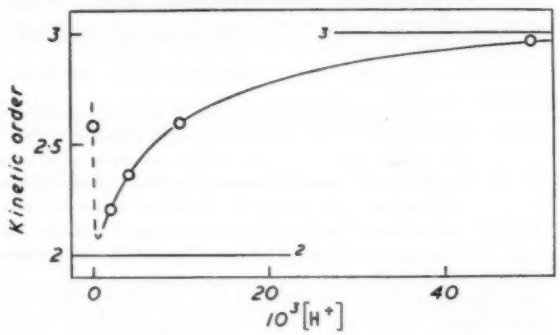


FIG. 2. *Diazotisation of aniline: overall kinetic order as a function of the excess of perchloric acid concentration.*



order, but it serves as a simple check of the large differences here under consideration. With no excess of acid, $\bar{k}_2$ falls and $\bar{k}_3$ rises in the course of the run. With 0·002M-acid, $\bar{k}_2$ remains constant, whilst $\bar{k}_3$ rises strongly. With 0·050M-acid, $\bar{k}_2$ falls strongly, whilst $\bar{k}_3$ remains steady.

We interpret these results as follows. At all acidities from 0·050M down to 0·002M, the concentrations of hydrogen ion can be taken as approximately constant throughout any

TABLE 1. *Diazotisation of aniline in dilute perchloric acid at 0°. Reactant half-life (min.) as a function of initial reactant concentration.*

Run	Free [H^+]	Stoicheiometric [$Ar{\cdot}NH_3^+$] = [HNO_2]	Half-life	Run	Free [H^+]	Stoicheiometric [$Ar{\cdot}NH_3^+$] = [HNO_2]	Half-life
47	0·000	0·0010	97·5	25	0·004	0·0015	22·2
21	,,	0·0020	31·5	26	,,	0·0020	15·2
45	,,	0·0020	32·5	27	,,	0·0030	8·6
20	,,	0·0027	20·0	28	0·010	0·0015	29·3
19	,,	0·0040	10·8	29	,,	0·0020	18·0
49	0·002	0·0010	38·3	30	,,	0·0030	9·4
44	,,	0·0020	16·1	182	0·050	0·0015	65·0
23	,,	0·0020	17·1	180	,,	0·0020	35·5
48	,,	0·0030	10·1	181	,,	0·0030	16·6

one run. Hence the concentration of either reactant in its uncharged molecular form will be a constant fraction of the stoicheiometric concentration of the reactant throughout any one run. It follows that the stoicheiometric second- or third-order rate-constants calculated

for any run are proportional to the corresponding molecular rate constants (cf. Part I, section 3c): constancy or drift in the molecular rate-constants will be reproduced faithfully in the stoicheiometric constants. It follows also that the reaction orders, computed as they have been from the manner of diminution of the stoicheiometric concentrations of the reactants, are the same as if they had been computed from the rates of disappearance of the reactants in their uncharged molecular forms. We conclude that the fall of reaction order, which can be traced over the greater part of Fig. 2, from approximately 3 at 0·050M-acid to near 2 at 0·002M-acid, owes nothing to the acid–base equilibria to which the reactants are subject. It must therefore be of primary significance for the mechanism of diazotisation.

On the other hand, when the excess of perchloric acid is removed completely, the concentration of hydrogen ions does not remain constant in a run: two weak acids, the anilinium ion and nitrous acid, are being replaced by a neutral diazonium ion and water; and hence the pH will rise. Of the two weak acids, nitrous acid is the stronger, and hence

TABLE 2. *Diazotisation of aniline in aqueous perchloric acid at* 0°. *Variations of integrated stoicheiometric, second- and third-order rate-constants during the progress of runs at different acidities.*

Run 47
[Reactants] = 0·001M. [Acid] = nil.

t (min.)	Reaction (%)	$\bar{k}_2$ (sec.$^{-1}$ mole^{-1} l.)	$\bar{k}_3$ (sec.$^{-1}$ mole^{-2} l.^{2})
0	7·0	—	—
15	20·0	0·195	222
25	26·5	0·190	230
35	32·0	0·188	238
45	37·5	0·195	260
55	40·0	0·178	245
75	46·0	0·172	252
95	50·3	0·163	253
115	54·0	0·157	258

Run 49
[Reactants] = 0·001M. [Acid] = 0·002M.

t (min.)	Reaction (%)	$\bar{k}_2$ (sec.$^{-1}$ mole^{-1} l.)	$\bar{k}_3$ (sec.$^{-1}$ mole^{-2} l.^{2})
0	13·0	—	—
5	21·5	0·417	503
10	29·5	0·448	583
15	35·3	0·440	593
20	40·0	0·430	608
25	44·5	0·435	640
35	51·0	0·423	677
45	55·0	0·397	672
55	60·0	0·410	745
65	63·5	0·408	793

Run 181
[Reactants] = 0·003M. [Acid] = 0·050M.

t (min.)	Reaction (%)	$\bar{k}_2$ (sec.$^{-1}$ mole^{-1} l.)	$\bar{k}_3$ (sec.$^{-1}$ mole^{-2} l.^{2})
0	21·0	—	—
3	31·7	0·367	167
6	39·1	0·348	167
9	43·8	0·315	158
12	47·9	0·303	162
17	53·3	0·287	153
22	57·4	0·272	163
27	60·4	0·258	163
32	63·2	0·255	168
37	65·1	0·242	168
42	66·9	0·230	163

will be neutralised first. And thus the first effect of the rising pH will be to replace nitrous acid by nitrite ion in increasing proportions. The concurrent replacement of anilinium ion by molecular aniline has no comparable, countervailing, kinetic effect for a reason which will appear below. Hence the shift in the acid–base equilibria as reaction progresses will lead to a growing retardation, and this will show itself as an enhancement of kinetic order. It is possible thus to account for the rise of overall order to about 2·6 as the last of the excess of strong acid is removed. Therefore this change, shown on the extreme left of Fig. 2, has no primary significance for the mechanism of diazotisation.

(2) *Detailed Kinetics of the Second-order Reaction.*—Concerning the distribution of kinetic order between the reactants, the third-order reaction has already been examined by Schmid (cf. Part I, section 2), who found its kinetic form to be identical with that previously established by Taylor for the reaction of nitrous acid with other types of amine. With

our convention (Part I, section 1c) of attaching a literal rather than an analytical meaning to bracketed symbols, this equation takes form (1):

$$\text{Rate} = k_3''[\text{Ar}\cdot\text{NH}_2][\text{HNO}_2]^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

As to the second-order reaction, Hantzsch and Schumann originally assigned a unit of kinetic order to each reactant, but without experimental proof, and presumably because they could imagine no alternative (cf. Part I, section 2). This assignment, represented in

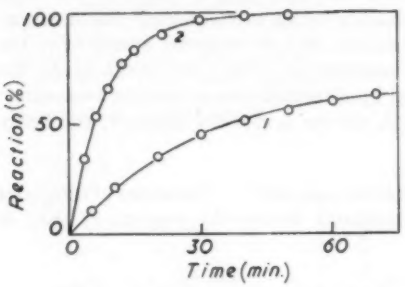


FIG. 3. *Effect of nitrous acid concentration on the rate of second-order diazotisation in aqueous perchloric acid at 0°.*

Stoicheiometric concentrations:

1, *Initially,*
$[\text{Ar}\cdot\text{NH}_3^+] = 0{\cdot}001$, $[\text{HNO}_2] = 0{\cdot}001$, $[\text{H}^+] = 0{\cdot}002$M.

2, *Initially,*
$[\text{Ar}\cdot\text{NH}_3^+] = 0{\cdot}001$, $[\text{HNO}_2] = 0{\cdot}002$, $[\text{H}^+] = 0{\cdot}002$M.

our terminology by equation (2), had been neither proved, nor specifically questioned, since then:

$$\text{Rate} = k_2'[\text{Ar}\cdot\text{NH}_2][\text{HNO}_2] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

Therefore we next took up experimentally the matter of the distribution of order in this reaction.

A series of experiments with the same initial stoicheiometric concentration of nitrous acid, 0·001M, and the same excess of perchloric acid, 0·002M, but with initial concentrations of anilinium perchlorate varying over a 10-fold range, gave reaction rates which were, to within 20%, the same, as shown in Table 3. Obviously, the kinetic order in aniline was zero substantially, and therefore the order in nitrous acid had to be two. We concluded that the correct equation for the second-order reaction was (3):

$$\text{Rate} = k_2''[\text{HNO}_2]^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

This was confirmed by duplicating two of the runs (nos. 49 and 50), but with a doubled initial concentration of nitrous acid: the runs then went four times as fast, as illustrated for one case in Fig. 3.

TABLE 3. *Effect of aniline concentration on rate of second-order diazotisation in aqueous perchloric acid at 0°.*

	Run:	49	50	56	55
Stoich. initial concns.	$[\text{Ar}\cdot\text{NH}_3^+]$	0·001	0·002	0·005	0·010
	$[\text{HNO}_2]$	0·001	0·001	0·001	0·001
	$[\text{H}^+]$	0·002	0·002	0·002	0·002
Time (min.)		Percentage reaction			
10		21·5	24·0	25·3	26·0
20		35·3	38·4	41·0	41·0
30		44·5	48·3	50·7	51·0
40		51·0	55·4	57·5	58·0
50		55·0	61·0	63·0	63·7
60		60·0	65·0	67·2	68·0
70		63·5	69·0	70·8	71·0

Final confirmation of the need to change the older view of the second-order reaction was obtained by calculating integrated, stoicheiometric, second-order rate-constants, $\bar{k}_2'$ and $\bar{k}_2''$, corresponding to equations (2) and (3), respectively. The behaviour of these

constants in the course of a run, one of such a kind that the choice of equation is critical, inasmuch as the reactants are out of stoicheiometric equivalence, is illustrated in Table 4: obviously, equation (2) is invalid, whilst equation (3) is valid.

(3) *The Absence of Hydrogen-ion Catalysis.*—Equation (3) is a correct expression of the second-order reaction, but it remains to be proved that it is complete. What has not yet been discussed is the dependence of the second-order rate-constant on acid, a question not raised by an examination of the kinetics of any one run, or by comparisons of rates among different runs at the same acidity. Obviously the degree of acidity must affect the rate

TABLE 4. *Stoicheiometric rate-constants (sec.$^{-1}$ mole^{-1} l.), calculated according to alternative second-order equations, for the diazotisation of aniline in aqueous perchloric acid at* 0°.

Run 50.—Stoicheiometric initial concentrations: $[Ar{\cdot}NH_3^+] = 0{\cdot}002$, $[HNO_2] = 0{\cdot}001$, $[H^+] = 0{\cdot}002$M.

t (min.)	Reaction (%)	$\bar{k}_2'$ (eqn. 2)	$\bar{k}_2''$ (eqn. 3)	t (min.)	Reaction (%)	$\bar{k}_2'$ (eqn. 2)	$\bar{k}_2''$ (eqn. 3)
0	24·0	—	—	40	61·0	0·180	0·517
10	38·4	0·208	0·513	50	65·0	0·170	0·513
20	48·3	0·198	0·513	60	69·0	0·167	0·512
30	55·4	0·195	0·512	70	71·5	0·158	0·522

by its control of acid–base equilibria (Part I, section 3c) in which the reactants are involved in particular, nitrous acid, the kinetically significant reactant for the second-order reaction. But the point to be determined is whether, when this has been allowed for, a dependence on acid remains, which should be expressed by some definite kinetic order in hydrogen ions.

Experiments have therefore been carried out to determine the dependence of the second-order rate-constants on acid concentration, and the results are in Table 5. The stoicheiometric rate-constants $\bar{k}_2''$ show an appreciable positive dependence on acidity, though it is very much less than would correspond to a unit of kinetic order in hydrogen ions. When we calculate the more significant molecular rate-constants k_2'', the greater part of the dependence on acid drops away, leaving only 15% of change for a 10-fold change in acidity. It is therefore clear that equation (3) is complete as it stands, and that it represents a process which is not catalysed by hydrogen ions.

TABLE 5. *Acid-dependence of the second-order (equation* 3) *stoicheiometric ($\bar{k}_2''$) and molecular (k_2'') rate-constants (sec.$^{-1}$ mole^{-1} l.) for the diazotisation of aniline in aqueous perchloric acid at* 0°.

Initially added, $[Ph{\cdot}NH_3^+ClO_4^-] = 0{\cdot}01$, and $[HNO_2] = 0{\cdot}001$M, throughout. (Molecular rate-constants are calculated by assuming the acidity constant of nitrous acid to be $4{\cdot}5 \times 10^{-4}$ mole l.$^{-1}$. The above stoicheiometric concentration of aniline is sufficient to secure second-order kinetics at all the following acidities.)

Run	55	183	184	185
$[H^+]$	0·002	0·009	0·014	0·019
$\bar{k}_2''$	0·583	0·837	0·923	0·938
k_2''	0·867	0·925	0·983	0·983

The cause of the small increase in the molecular rate-constant with increasing acidity cannot be settled unambiguously on the basis of the data in this paper. The drift as calculated depends on the value taken for the acidity constant of nitrous acid, and also on the changes in activity coefficients with ionic strength. However, we may be seeing signs here of a small acid-catalysed component of the observed reaction. For this reason, the true value of the second-order rate-constant k_2'' is a little uncertain, but, given that the acidity constant of nitrous acid may be taken as $4{\cdot}5 \times 10^{-4}$ mole l.$^{-1}$, the data of Table 5 allow us to assign to k_2'' the approximate value 0·85 sec.$^{-1}$ mole^{-1} l.

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XUM

15. *Nitrosation, Diazotisation, and Deamination. Part III.* Zeroth-order Diazotisation of Aromatic Amines in Carboxylic Acid Buffers*

By E. D. Hughes and J. H. Ridd.

The diazotisation of aniline in acetate and phthalate buffers near pH 5, with a constant excess of nitrous acid, follows linear reaction–time curves until the falling concentration of aniline approaches 10^{-5}M. At higher aniline concentrations, the kinetic order is 0 in aniline; and, by comparisons among different runs, it is shown to be 1·8 in nitrous acid, the defect below 2 being explicable as a buffer disturbance. The zeroth-order law applies, not only to aniline, but also to substituted anilines with pK_a greater than about 4, which all undergo diazotisation at the same absolute rate. But for more weakly basic aniline derivatives the rate falls, and a non-zero order in amine enters, these effects increasing as the basic strength is diminished. Analogies with previous investigations on nitration and chlorination are pointed out.

In first approximation, acetate and phthalate buffers do not change the kinetic orders in amine or nitrous acid, but a part of the rate in their presence is represented by a catalytic term of first order in buffer anion. There is probably a superposed small disturbance, of a type serious with some other buffers and characterised by a loss of kinetic order in nitrous acid in substitution for an introduced non-zero order in buffer acid (cf. halide catalysis, Part V of this series).

In the experiments recorded in Part II * on the diazotisation of aniline in dilute aqueous perchloric acid, it was not possible to bring the overall kinetic order from 3 completely down to 2 by progressively reducing the concentration of the excess of perchloric acid, because, when this excess became reduced below 0·002M, the acid–base equilibria in which the reactants are involved become shifted as reaction progresses in such a way as to produce an appreciable increase in apparent kinetic order. For the purpose of setting a steady acidity much lower than the rough limit indicated, one has to have recourse to buffers.

A further consideration indicated the need for work in this direction. As we shall see in Part VI, the group of kinetic results assembled in Part II contains one finding of outstanding importance, *viz.*, that the second-order reaction is of zeroth order in aniline. This proves that a purely inorganic reaction of nitrous species is involved, which is of such a nature that it can become rate-controlling; and this in turn proves the nitrosation mechanism, just as, in the past, observations on nitration, and on chlorination, of zeroth order in what was being nitrated or chlorinated, established mechanisms of substitution by the nitronium ion and the chlorinium ion. Obviously it was important to demonstrate the zeroth order clearly, and, having in mind particularly the model provided by the previous demonstration concerning nitration,[1] we wished to exhibit zeroth-order diazotisation by having nitrous acid in constant excess and obtaining a rectilinear reaction–time curve, which should be the same for all sufficiently reactive amines, though this uniform simplicity should break down in a characteristic way as the reactivity of the amine is reduced. The difficulty of fulfilling this programme, by the technique of Part II, is that, in excess of perchloric acid, the nitrous acid is nearly all in non-ionised form, and the necessary excessive concentration of it, 0·01M or more, is so large as to render diazotisation too rapid for easy measurement. Now this difficulty can be overcome by carrying out diazotisations in solutions buffered at about pH 5. At this pH, most of the nitrous acid is in ionised form, with the result that a considerable stoicheiometric concentration involves only a small molecular concentration, wherefore, even with 0·01M stoicheiometric nitrous

* Part II, preceding paper.

[1] Benford and Ingold, *J.*, 1938, 929; Hughes, Ingold, and Reed, *Nature*, 1946, **158**, 448; *J.*, 1950, 2400.

acid, the rate of diazotisation can be kept down to easily measurable values. At the same time, by virtue of the buffering, the molecular concentration of nitrous acid remains a constant fraction of its stoicheiometric concentration, so that if the latter is in constant excess, the former is constant.

A decision to use buffers involves an investigation into the suitability of possible buffers. For we must expect that, in general, buffer anions will disturb diazotisation, and it is therefore necessary to ensure that any such disturbance does not upset what is to be demonstrated. Now a buffer anion might conceivably disturb diazotisation kinetics in either of two ways. First, it might catalyse the formation of that nitrosating entity which would have operated in its absence, and *a fortiori* operates also in its presence. Secondly, it might produce a new and more active nitrosating entity. The problem, then, is to choose a buffer which does not act in the second of these ways, or, to put it more practically, one which, even if it catalyses the measured reaction, does not otherwise change its kinetic form. The required conditions were found to be fulfilled by acetate and phthalate buffers. (They are not fulfilled by phosphate buffers, which have, uncircumspectly, been employed in related reactions by other workers—cf. Part VI.) Some further details of this ancillary investigation are given in section 4.

(1) *Diazotisation of Aniline: Kinetic Order with Respect to Aniline.*—When acetate and phthalate buffers are used near pH 5 and in 20-fold stoicheiometric excess of nitrous acid over amine, zeroth-order reaction–time curves have been obtained for aniline and for several other aromatic amines. Some data for aniline are recorded in Table 1, and the graphs obtained are shown in Fig. 1.

TABLE 1. *Diazotisation of aniline in aqueous buffers at* 0°.

Initially added, $[Ph{\cdot}NH_3^+ClO_4^-] \doteq 0{\cdot}0005$, $[NaNO_2] = 0{\cdot}01$, and either [sodium acetate + acetic acid] or [sodium potassium phthalate + potassium hydrogen phthalate] = 0·05M.

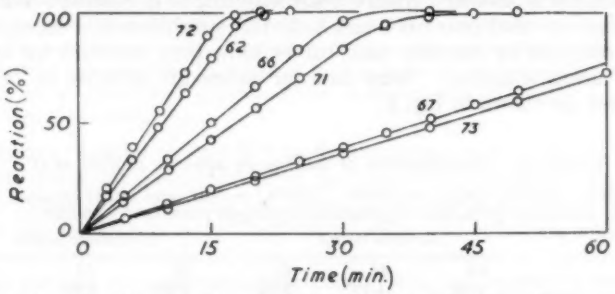
	Acetate buffer			Phthalate buffer		
Run	62	66	67	72	71	73
pH	4·63	4·77	5·02	4·80	5·00	5·20
Time (min.)	Reaction (%)					
3	16·0	—	—	19·8	—	—
5	—	16·8	—	—	14·6	6·4
6	33·2	—	—	38·2	—	—
9	47·8	—	—	56·2	—	—
10	—	33·4	12·0	—	28·8	13·0
12	63·4	—	—	73·0	—	—
15	78·8	50·0	—	88·6	42·0	20·0
18	92·8	—	—	98·6	—	—
20	—	66·0	24·2	—	56·8	26·2
21	99·8	—	—	100	—	—
24	100	—	—	100	—	—
25	—	82·8	—	—	70·4	33·4
27	—	—	—	—	—	—
30	—	95·2	36·4	—	83·0	39·0
35	—	—	—	—	93·0	45·8
40	—	100	47·2	—	97·0	52·2
45	—	—	—	—	99·2	58·8
50	—	—	59·2	—	99·2	64·2
60	—	—	70·4	—	—	—

It is clear that, over nearly the whole of these runs, the kinetic order in aniline is zero. A deviation occurs above 95% reaction, when the concentration of aniline is becoming very low. At pH 5, the aniline is present almost entirely in the form of free base, and at 95% reaction, both the stoicheiometric and (what really matters) the molecular concentration of aniline is approaching 10^{-5}M. We can understand the kinetic deviation in this region as the onset of transition from overall second-order to third-order kinetics (Part II). It is to be compared with what happens when, in the experiments on diazotisation in

perchloric acid (Part II), we increase the excess of acid, thereby cutting down the concentration of molecular aniline. Here also the kinetic transition takes place when the concentration of molecular aniline becomes reduced to the order of magnitude 10^{-5}M.

(2) *Diazotisation of Aniline: Kinetic Order with Respect to Nitrous Acid.*—It is necessary to check the order in nitrous acid, and since nitrous acid is in constant excess, this has to be done by comparing one run with another. We can change the concentration of molecular nitrous acid from run to run by changing the pH, and keeping constant the stoicheiometric concentration of nitrous acid. In our pH range, a few units per cent. of the stoicheiometric nitrous acid are present in molecular form, and we change this percentage when we change the pH. The data for a test of this nature are in Table 1. Because of the specific effect of the buffer components, we must compare runs with the same buffer in the same concentrations, and such comparisons lead, as will be illustrated, to a kinetic order in molecular nitrous acid of approximately 2. However, this result alone would leave a sense of doubt, because, in changing the pH, we have to change the buffer ratio, and this might modify the specific kinetic effect of the buffer.

FIG. 1. *Zeroth-order reaction–time curves for the diazotisation of aniline with excess of nitrite in acetate or phthalate buffers at* pH 4·6—5·2. (*The figures against the curves are run numbers as in Table* 1.)



It seems a safer plan to vary the concentration of molecular nitrous acid by holding the pH constant and changing the stoicheiometric concentration of nitrous acid. A series of experiments have been conducted on these lines. In them the pH was buffered at 5·0 with 0·05M-phthalate buffer, and the concentration of initially added sodium nitrite was changed from run to run. The results are given in Table 2, along with those of the previously mentioned experiments in phthalate buffer in which the pH was changed and the concentration of added sodium nitrite was kept constant.

TABLE 2. *Dependence of zeroth-order rates (mole* $l.^{-1}$ *sec.*$^{-1}$*) of diazotisation of aniline in* 0·05M-*phthalate buffer at* 0° *on the concentration of molecular nitrous acid.*

Run	pH	Added [$NaNO_2$] (10^{-3}M)	Added [$Ph{\cdot}NH_3^+ClO_4^-$] (10^{-3}M)	Molecular [HNO_2] * (10^{-3}M)	$10^6 k_0$
73	4·8	10	0·5	0·138	0·108
71	5·0	,,	0·5	0·218	0·240
72	5·2	,,	0·5	0·340	0·530
82	5·0	5	0·1	0·109	0·061
94	,,	10	0·5	0·218	0·247
93	,,	13·3	0·5	0·290	0·325
95	,,	15·4	0·5	0·336	0·485

* Calculated by taking the acidity constant of nitrous acid to be $4{\cdot}5 \times 10^{-4}$ mole $l.^{-1}$.

When the sets of figures in the last two columns of Table 2 are plotted on a logarithmic scale, the points, no matter whether they are related through variations of pH, or through variations in the stoicheiometric concentration of nitrous acid, lie about a common straight line of slope 1·8, as is shown in Fig. 2. This slope represents the kinetic order with respect to nitrous acid.

The observed small defect below the integral kinetic order of two may be real, and may be the measure of one's failure to find buffers which would not produce specific nitrosating agents of reactivity appreciable in comparison with that of those nitrous species which effect nitrosation in the absence of buffers and are still of main importance in the buffers. If nitrosyl acetate or nitrosyl phthalate were to be formed, and were to become dominating nitrosating agents, the kinetic order in nitrous acid should fall to unity; and if such buffer-derived nitrosating agent were formed sufficiently quickly, the kinetic order in aniline should rise to unity. In fact, the order in aniline remains zero, and that in nitrous acid falls only a little below two. This shows that we are at least not changing the main nitrosating agent when we work in these particular buffers.

(3) *Diazotisation of Various Aromatic Amines.*—The kinetic order of zero with respect to aniline must mean that the aniline is reacting instantly with a slowly formed nitrosating agent. When we follow overall second-order diazotisation, we measure the purely inorganic process leading to this reagent. Therefore any amine which (*a*) is present in sufficient concentration, and (*b*) has a sufficient specific activity to take up the reagent as fast as it is produced, should react according to the same kinetic law, and at the same

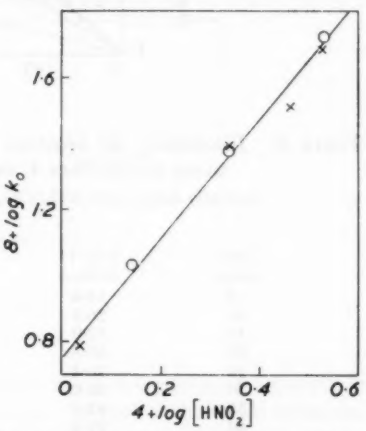


FIG. 2. *Logarithmic plot of the zeroth-order rate of diazotisation of aniline in phthalate buffers* versus *the concentration of molecular nitrous acid.*

○, *Points related by variation of* pH. × *Points related by variation in the stoicheiometric concentration of nitrous acid. The straight line has the slope* 1·8.

absolute rate, as aniline. This statement should hold generally for primary and secondary, aliphatic and aromatic, amines: indeed, it need not be confined to amines. In relation to the conditions of the present diazotisations in buffers, aromatic primary amines are in a simple position as regard supply, inasmuch as their molecular concentrations are practically equal to their stoicheiometric concentrations, which one may directly control and keep comparable. As regards specific reactivity, basic strength will serve as a qualitative guide. The pK_a values of the conjugate acids of the amines to be compared in this section, are given below:

R in R·C$_6$H$_4$·NH$_2$	*p*-Me	*m*-Me	H	*o*-Me	*p*-Br	*m*-Br	*o*-Br
pK_a	5·07	4·69	4·58	4·39	3·94	3·51	2·60

The identity of diazotisation rate for aniline and the three toluidines is shown in Table 3. All these diazotisations follow the same reaction–time curve; and this common curve is a straight line up to 95% reaction, like the curves shown in Fig. 1. In these experiments, as in those of Table 1 and Fig. 1, the initial amine concentration was 0·0005M.

On going to successively weaker bases, we must expect sooner or later to reach a point at which this simple relation breaks down, because the aromatic amine is insufficiently reactive to take up the nitrosating agent as fast as the latter is formed. Such a point is reached when the pK_a value of the conjugate acid of the amine drops below about 4.

This is shown in the experiments recorded in Table 4. In these the initial amine

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concentration was lowered to 0·0001M, and because of this more restricted supply of amine, the linear law for aniline now holds up to about 75% reaction. However, the restricted supply brings into greater relief the effects of base-weakness, as seen in Fig. 3. *p*-Bromoaniline is diazotised appreciably more slowly than aniline, though one can only with difficulty in this case detect the incipient change of kinetic form. But *m*-bromoaniline, and still more *o*-bromoaniline, are diazotised much more slowly, and their reaction–time curves depart detectably from linearity, even up to 40—50% of reaction.

FIG. 3. *Reaction–time curves for the diazotisation of aniline and the three bromoanilines with excess of nitrite in a phthalate buffer at* pH 5.

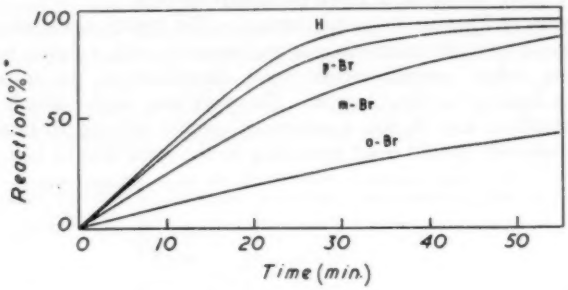


TABLE 3. *Illustrating the identical diazotisation rates of aromatic amines, having* pK_a *values greater than* 4, *in a* 0·05M-*phthalate buffer of* pH 5 *at* 0°.

(Initially added, $[Ar{\cdot}NH_3^+ClO_4]^- = 0{\cdot}0005$, and $[NaNO_2] = 0{\cdot}01$M throughout.)

Time (min.)	Reaction (%) Run 71 Aniline	Run 76 *o*-Toluidine	Run 75 *m*-Toluidine	Run 74 *p*-Toluidine
5	14·6	14·8	14·4	14·4
10	28·8	29·4	29·6	28·4
15	42·0	44·0	43·0	42·8
20	56·8	57·2	57·4	56·8
25	70·4	70·6	70·6	70·4
30	83·0	82·4	82·6	82·8
35	93·0	92·6	93·8	93·8
40	97·0	98·8	99·0	99·0
45	99·2	100·0	100·0	100·2
50	99·2	99·8	99·8	99·8

TABLE 4. *Deviations from the common diazotisation rate, represented by that of aniline, shown by amines with* pK_a *values less than* 4, *in a* 0·05M-*phthalate buffer of* pH 5 *at* 0°.

(Initially added, $[Ar{\cdot}NH_3^+ClO_4^-] = 0{\cdot}0001$ and $[NaNO_2] = 0{\cdot}005$M, throughout.)

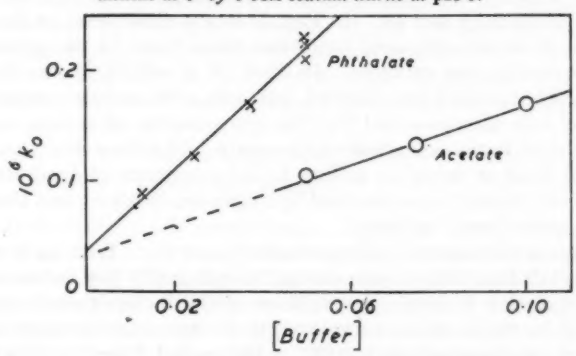
Time (min.)	Reaction (%) Run 82 Aniline	Run 83 *p*-Bromo-	Run 85 *m*-Bromo-	Run 84 *o*-Bromo-
5	18·1	17·1	12·8	—
10	36·8	34·2	25·0	9·1
15	53·5	50·8	36·4	—
20	69·5	64·0	46·6	17·4
25	80·5	74·0	56·0	—
30	88·0	80·5	63·5	25·8
35	91·5	84·0	69·5	—
40	91·5	87·5	74·2	32·6
45	92·5	89·5	78·4	—
50	94·0	90·0	82·4	40·0

The phenomenon under observation here is of the kind already known in aromatic nitration with excess of nitric acid: when the reactivity of the aromatic compound is progressively reduced, the previously coincident and rectilinear reaction–time curves

(*a*) lose slope, (*b*) separate from one another, and (*c*) bend, as a reaction of zeroth order in the aromatic compound goes over into a reaction of first order.[1] The interpretation is the same in that case as in the present one of diazotisation. It is that a preliminary inorganic-chemical process is required to produce the effective agent, and that this process is just sufficiently slow enough for it to be rate-controlling or not, according to the reactivity of what is available to interact with the reagent formed.

(4) *Catalysis of Diazotisation by Buffer Components.*—Although the buffers here used do not change the kinetic order, either in the amine or in the nitrous acid, they do supply a catalysis. This is evident from the fact that, at the same pH, diazotisation in a phthalate buffer is faster than in an acetate buffer (cf. the curves for runs 67 and 73 in Fig. 1); and also from the fact that, in both these buffers, diazotisation is faster than it is in the absence of a buffer, but in perchloric acid of such low concentration as to produce the second-order reaction (Part II). Presumably the specific acceleration in buffers is due to catalysis by the buffer anion of the rate-controlling step of second-order diazotisation, or, in other

FIG. 4. *Catalysis by buffer components, at constant ionic strength, of the zeroth-order diazotisation of aniline at* 0° *by* 0·01M-*sodium nitrite at* pH 5.



words, catalysis of the formation of the same nitrosating agent as would have been effective in the absence of the buffer. A considerable fraction of the rate in the buffer solutions is due to such catalysis.

It is not necessary to describe the routine examination for specific effects of all the buffers considered, but in Table 5 some data are recorded for the buffers used, because the figures allow rate-equations and rate-constants to be deduced for both the uncatalysed and the buffer-catalysed processes. Some of the figures are zeroth-order rates of diazotisation of aniline by nitrous acid in the constant stoicheiometric concentration 0·01M, in a series of acetate buffers, all at pH 5, but with various concentrations of buffer, yet all at the constant ionic strength 0·1M, made up as necessary by the addition of sodium perchlorate. The rest of the figures refer to similar experiments with phthalate buffers, also at pH 5, but with various buffer concentrations, and made up to an ionic strength of 0·1M by means of sodium perchlorate. This method standardises the general salt effect,

TABLE 5. *Zeroth-order rates (mole* $l.^{-1}$ *sec.*$^{-1}$*) of diazotisation of aniline by a constant excess of nitrous acid in buffers at* pH 5 *but in various concentrations and at* 0°.

Initially added, $[Ph{\cdot}NH_3{}^+ClO_4{}^-] = 0{\cdot}0005$, and $[NaNO_2] = 0{\cdot}01$M, in all runs. Acetate and phthalate buffers were made up with $NaClO_4$ to ionic strength 0·10M.

Acetate	[Buffer]	0·050		0·075	0·100	
	$10^6 k_0$	0·100	0·104	0·130	0·168	
Phthalate	[Buffer]	0·0125	0·0250	0·0375	0·0500	
	$10^6 k_0$	0·089	0·124	0·168	0·211	0·222 0·229

which is probably retarding, and isolates the specific accelerating effects of the buffer components.

As can be seen from the graphs of these results in Fig. 4, buffer catalysis is linear in buffer concentration. Neither the uncatalysed nor the catalysed part of the rate is negligible.

We have to combine this result with those reported in the preceding sections. It was there shown that, for the diazotisation of aniline, and of other primary aromatic amines of similar or greater basic strength, in carboxylate buffers at or near pH 5, the overall rate is of zeroth order in aromatic amine and of second order in nitrous acid. These findings must apply to both the uncatalysed and the catalysed part of the rate. Thus we can summarise the combined results of this paper in equations (1) and (2):

$$\text{Uncatalysed rate} = k_2''[HNO_2]^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$\text{Catalysed Rate} \quad = k_3^{OAcyl}[OAcyl^-][HNO_2]^2 \quad . \quad . \quad . \quad . \quad . \quad (2)$$

In equation (2), the dependence of the catalysed rate on buffer is expressed in terms of buffer anion, because the alternatives of dependence on buffer acid can be excluded on the evidence of Parts II and IV. In Part II it was shown that in the diazotisation of aniline in much more strongly acid conditions than those of the present experiments, there is no appreciable acid catalysis. In Part IV it will be shown that hydrogen-ion catalysis in diazotisation can be observed, but only with amines considerably less basic than aniline, and only then provided that the concentration of nitrous acid is so reduced as to suppress kinetic forms dependent on its square. It is thus clear that, in the diazotisation of bases at least as strong as aniline, in the conditions of quadratic dependence of rate on nitrous acid, there is no substantial hydrogen-ion catalysis, and therefore, *a fortiori*, there can be no general acid catalysis.

We can compute the constants of equations (1) and (2). First, as to equation (1), the experiments in phthalate buffers were carried to sufficiently low buffer concentrations to justify an extrapolation to zero concentration of the buffer, though the relevant ionic strength will still be the common ionic strength in this series of experiments, *viz.*, 0·1M. The extrapolated zeroth-order rate is $0{\cdot}037 \times 10^{-6}$ mole $l.^{-1}$ $sec.^{-1}$. This figure applies to diazotisation by a concentration of molecular nitrous acid determined jointly by the stoicheiometric concentration of the nitrous acid and the pH. If we may take the acidity constant of nitrous acid as $4{\cdot}5 \times 10^{-4}$ mole $l.^{-1}$, the concentration of molecular nitrous acid is calculated to be $0{\cdot}218 \times 10^{-3}$M. By dividing the zeroth-order constant by the square of this concentration, we obtain the second-order rate-constant k_2'' for diazotisation according to equation 1. The value is 0·78 $sec.^{-1}$ $mole^{-1}$ l. This applies to an ionic strength of 0·1M.

From the dependence on acid of the stoicheiometric second-order rate-constants, observed for diazotisation in small excesses of perchloric acid, it was computed in Part II, again on the assumption that the acidity constant for nitrous acid may be taken as $4{\cdot}5 \times 10^{-4}$ mole $l.^{-1}$, that the molecular second-order rate-constant k_2'' is close to 0·85 $sec.^{-1}$ $mole^{-1}$ l. This applies to low ionic strengths. The agreement with the constant deduced by extrapolation from rates in buffers is satisfactory.

In order to obtain the values of the constant k_3^{OAcyl} of equation (2), we have to divide the slopes of the curves in Fig. 4, first by the mole-fraction of anion in the acetate buffer, or of bivalent anion in the phthalate buffer, and then by the square of the concentration of molecular nitrous acid, calculated as before. The result for acetate ion is 38 $sec.^{-1}$ $mole^{-2}$ $l.^2$; and for phthalate ion it is 160 $sec.^{-1}$ $mole^{-2}$ $l.^2$.

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16. *Nitrosation, Diazotisation, and Deamination. Part IV.* Hydrogen-ion Catalysis in the Diazotisation of o-Chloroaniline in Dilute Perchloric Acid.*

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Diazotisation rates were sometimes observed which were greater than those prescribed by the kinetic equations of the preceding papers; a study of the discrepancies revealed that they were due to an additional diazotisation process, which could be made dominating with an amine of suitable basicity, by operating in a suitable range of acidity, with a very low concentration of nitrous acid. This new process was examined in detail for *o*-chloroaniline in perchloric acid in 0·005—0·020M-excess, with nitrous acid in concentrations below 0·0001M. The reaction was shown to be of first order each in hydrogen ions, in amine, and in nitrous acid.

(1) *The Detection of Acid-catalysis.*—When the concentration of aniline in free-basic form is increased by a progressive reduction of acidity, the rate of diazotisation, with a constant concentration of molecular nitrous acid, at first increases proportionally to the concentration of free base, then begins to increase more slowly, and finally attains a constant maximum. The first situation is represented by equation (1), and the last by equation (2), where the bracketed quantities mean molecular, rather than stoicheiometric, concentrations:

$$\text{Rate} = k_3''[\text{Ar}\cdot\text{NH}_2][\text{HNO}_2]^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$\text{Rate} = k_2''[\text{HNO}_2]^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

This was established in Part II particularly. It follows from it that other aromatic amines should be diazotised at rates, which at low acidities rise to the same upper limit, represented by equation (2). This conclusion was shown in Part III experimentally to have a certain range of validity. However, when the experimental work of Part II was repeated with other aromatic amines, the rates obtained were sometimes greater than the expected maximum rate given by equation (2). These discrepancies arose, or became more marked, when (*a*) the acidity was not excessively low, (*b*) the aromatic amine was a considerably weaker base than aniline, and (*c*) the concentration of molecular nitrous acid was excessively low. This suggests the incursion of another mechanism of diazotisation, one unconnected with kinetic equations (1) and (2). One can tentatively assign kinetic characteristics to the new mechanism: (*a'*) it is probably acid-catalysed; (*b'*) it probably has a kinetic order greater than zero in the aromatic amine; (*c'*) it certainly has a kinetic order less than two in the nitrous acid.

There is, of course, an interplay between effects (*a*) and (*b*), and between conclusions (*a'*) and (*b'*), an interplay expected to lead to optima. For example, if the new reaction were of first order in acid and first in amine, the acidity, which has to be low enough to give significance to the reference rate of equation (2), cannot be made indefinitely low if the new reaction is to appear, because even a maximum liberation of free-basic amine will be unable to compensate the kinetic effect of a vanishing acidity. Again, whilst it is important that the amine should be a weak enough base to be liberated appreciably at the allowable acidities, it must not be so weak, and hence so unreactive, that, even if liberated quantitatively, it produces a vanishing reaction rate by the new mechanism. Obviously the new reaction has to be of order lower than two in nitrous acid, so that it will be left in relative prominence, as the reaction of equation (2) dies out, when the concentration of nitrous acid is reduced.

It is implied in these conclusions that the "old" reaction, that governed by the limiting equations (1) and (2), and by the transitional kinetics bounded by them, and the

* Part III, preceding paper.

" new " reaction, that detected as described, must in principle go on together. Under the conditions of the experiments described in Parts II and III, the new reaction must have accounted for only a small proportion of the total rate, with the result that the old reaction stood sufficiently alone for kinetic elucidation. Our object was now to reverse these relations; *i.e.*, to reduce the old reaction to relative insignificance, and so kinetically to isolate the new reaction.

(2) *Isolation of Acid-catalysed Diazotisation.*—A preliminary survey, guided by these considerations, of the diazotisation of various aromatic amines led us to select for detailed study the diazotisation of *o*-chloroaniline, a base about 65 times weaker than aniline. We found it convenient to work in the acidity range 0·005—0·02M, maintained by suitable excesses of perchloric acid, and to employ nitrous acid initially in the very small stoicheiometric concentration 0·0001M.

Some explanation is necessary of the method of controlling acidity, since it was not, and could not be, the same as in the previously described experiments, on the diazotisation of aniline in perchloric acid. In those experiments, the concentration of hydrogen ions could be taken with sufficient approximation as equal to the stoicheiometric excess of perchloric acid. This was a legitimate simplification, because, at the relevant acidities, nitrous acid was too weak, and the anilinium ion much too weak, as an acid, to supply any important proportion of the hydrogen ions. However, the *o*-chloroanilinium ion is a considerably stronger acid, pK_a 2·77, and, in our acidity range, pH 1·7—2·3, it will be a significant contributor of hydrogen ions. Nitrous acid will remain negligible in this regard, largely because stoicheiometrically so little of it is present. Therefore, in order to keep a fixed hydrogen-ion concentration in a series of runs characterised by successively increased initial concentrations of *o*-chloroaniline, we have to compensate for the increased supply of hydrogen ions on account of increases in the concentration of *o*-chloroanilinium ion, by providing successively decreased stoicheiometric excesses of perchloric acid. The example given in Table 1 will make the method clear.

TABLE 1. *Control of hydrogen-ion concentration* (M) *in the diazotisation of* o-*chloroaniline.*

Run	151	154	124	123
[Stoicheiometric *o*-$Cl{\cdot}C_6H_4{\cdot}NH_3^+$]	0·0020	0·0040	0·0060	0·0080
[,, HNO_2]	0·0001	0·0001	0·0001	0·0001
[Neutralised * $HClO_4$]	0·0021	0·0041	0·0061	0·0081
[Excess of $HClO_4$]	0·0046	0·0041	0·0036	0·0031
[H^+]	0·0051	0·0051	0·0051	0·0051

* By initially added *o*-chloroaniline and sodium nitrite.

We have next to show that, under the conditions selected, the old reaction can indeed be made so subordinate as to leave the new reaction in isolation. Three runs with different stoicheiometric concentrations of *o*-chloroaniline, but with the same concentration of nitrous acid, and at the same acidity, are recorded in Table 2. It is clear from inspection of the plots in Fig. 1, that these runs have a finite kinetic order in *o*-chloroaniline. From the rate constant k_2'' of equation (2), as determined in Part II, and the molecular concentration of nitrous acid used in the present experiments, we can calculate the maximum rate, given by equation (2), of diazotisation by the old reaction, acting alone. This is represented by the full-line curve near the bottom of the diagram. Of course, it is the curve which would express reaction progress by this mechanism, if there were no other way than that of using up nitrous acid. In order to obtain a curve representing the extent to which the old reaction accompanies the new, we must reduce the slope of the curve for the old reaction in proportion to the square of the concentration of nitrous acid surviving the new. This is done for run no. 138, the run in which the old reaction has its greatest importance, in the broken line in Fig. 1. Clearly the old reaction is only of small importance (total 8%) even in this case. It will be negligible in most cases, and thus we can proceed to study the kinetics of the new mechanism with almost complete disregard of the old.

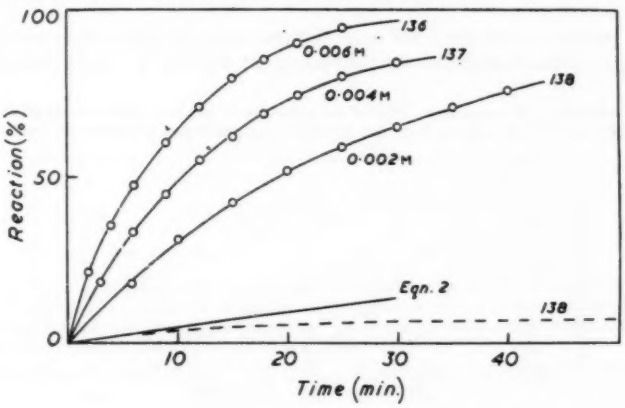
TABLE 2. *Course of the diazotisation of* o*-chloroaniline in water at* 0°.

Initially, $[HNO_2] = 0{\cdot}0001$, and $[H^+] = 0{\cdot}0204$M, throughout; whilst [stoicheiometric amine] is as follows: Run 136, 0·006M; run 137, 0·004M; run 138, 0·002M.

Run:	136	137	138	Run:	136	137	138
Time (min.)	Reaction (%)			Time (min.)	Reaction (%)		
2	21·0	—	—	15	79·5	61·5	42·5
3	—	18·0	—	18	85·3	68·5	—
4	35·0	—	—	20	—	—	51·3
5	—	—	17·0	21	90·0	74·3	—
6	47·3	33·7	—	25	94·5	80·0	58·5
9	60·0	44·5	—	30	—	84·5	65·0
10	—	—	31·5	35	—	—	71·2
12	71·0	54·2	—	40	—	—	76·0

(3) *Kinetics of Acid-catalysed Diazotisation.*—The data obtained for this purpose constitute a generalisation of those in Table 2. In all runs, the initial concentration of stoicheiometric nitrous acid was 0·0001M, and the amine was stoicheiometrically in

FIG. 1. *Diazotisation of* o*-chloroaniline with three initial stoicheiometric concentrations of amine (entered against the curves), and a common initial concentration of nitrous acid* 0·0001M *and a common acidity* (0·0204M). (*For interpretation of the bottom two lines see text.*)



constant excess. In the set of runs illustrated in Table 2, the initial stoicheiometric concentration of amine was changed from run to run, whilst the acidity was kept constant in the set. Several other sets of runs were done, within each of which the amine concentration was varied, whilst the acidity was kept constant within each set but was varied from set to set.

Since acid-catalysis is found to be involved in the new reaction, we have to keep clear the distinction between stoicheiometric and molecular rate-constants (Part I, section 3c). For the purpose of computing the latter from the former, we need to know the proportions in which nitrous acid and *o*-chloroaniline are present in molecular form at the different acidities used. Taking the acidity constant of nitrous acid as $4{\cdot}5 \times 10^{-4}$ mole l.$^{-1}$ and that of the *o*-chloroanilinium ion as $3{\cdot}6 \times 10^{-3}$ mole l.$^{-1}$, we obtain the values shown in Table 3, which have been used in the calculations.

TABLE 3. *Proportions in which nitrous acid and* o*-chloroaniline are present in molecular form at various acidities.*

$[H^+]$	0·0051	0·0102	0·0153	0·0204
Nitrous acid, non-ionised (%)	92	96	97	98
o-Chloroaniline as base (%)	25·0	14·3	10·0	7·7

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The results of these experiments are assembled in Table 4, where they are expressed in terms of rate-constants of various types, calculated as described below, with the aid, in some cases, of the data of Table 3.

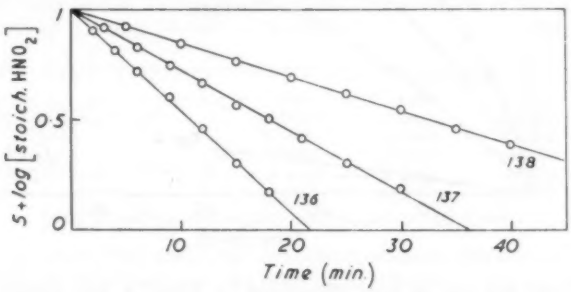
TABLE 4. *Rate-constants for the diazotisation of o-chloroaniline with a low concentration of nitrous acid in dilute aqueous perchloric acid at 0°.*

(Initial stoicheiometric concentration of nitrous acid 0·0001M throughout. Units: $\bar{k}_1'$ and k_1' in sec.$^{-1}$; $\bar{k}_2'$ and k_2' in sec.$^{-1}$ mole^{-1} l.; k_2^{H} in sec.$^{-1}$ mole^{-2} l.^{2}.)

Set	Run	[H$^+$]	[Stoich. amine]	Stoich. $10^3\bar{k}_1'$	Molr. $10^3k_1'$	Stoich. $10\bar{k}_2'$	Molr. $10k_2'$	Molr. $10^{-2}k_2^{H}$
1	123	0·0051	0·008	1·53	1·67	1·91	8·3	1·63
1	124	0·0051	0·006	1·15	1·25	1·86	8·1	1·59
1	154	0·0051	0·004	0·80	0·87	2·00	8·7	1·71
1	151	0·0051	0·002	0·47	0·50	2·35	10·6	2·08
2	132	0·0102	0·006	1·42	1·48	2·37	17·3	1·70
2	133	0·0102	0·004	0·97	1·00	2·42	17·6	1·73
2	134	0·0102	0·002	0·52	0·53	2·60	18·9	1·86
3	128	0·0153	0·006	1·52	1·57	2·53	26·0	1·70
3	130	0·0153	0·004	1·00	1·03	2·50	25·7	1·68
3	131	0·0153	0·002	0·53	0·55	2·65	27·2	1·78
4	136	0·0204	0·006	1·68	1·72	2·81	37·1	1·81
4	137	0·0204	0·004	1·08	1·10	2·70	35·8	1·76
4	138	0·0204	0·002	0·58	0·60	2·90	38·4	1·92

When the reaction–time data for any of these runs are plotted semilogarithmically, linear graphs are obtained as shown for the runs of set 4 in Fig. 2. This establishes that the

FIG. 2. *Diazotisation of o-chloroaniline: Plot of the logarithm of nitrous acid concentration* versus *the time for three runs at the same acidity but with different concentrations of amine in constant excess.*



new diazotisation process is of first order in nitrous acid. The slopes of the graphs give the stoicheiometric first-order rate-constants, $\bar{k}_1'$. From these, with the aid of Table 3, we can calculate the molecular first-order constants, k_1', that is, the true rate-constants of equation (3), which apply when the nitrous acid concentration is the only variable.

$$\text{Rate} = k_1'[\text{HNO}_2] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

When the stoicheiometric first-order rate-constants for any single set of runs are plotted against the (constant-excess) stoicheiometric concentrations of amine, a straight line is obtained, which passes through the origin. Similarly plotted, the data for the different sets of runs give different straight lines, all passing through the origin. This establishes that the reaction is of first order in amine. The slopes of the lines give the stoicheiometric second-order rate-constants $\bar{k}_2'$, and from these, by further use of Table 3, we can compute the molecular second-order constants k_2', that is, the true rate-constants of equation (4), which applies when the variable concentrations are those of the nitrous acid and the amine:

$$\text{Rate} = k_2'[\text{Ar·NH}_2][\text{HNO}_2] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

Alternatively, we may plot the molecular first-order rate-constant k_1' against the molecular concentration of amine, deduced with the help of Table 3, so obtaining a family of straight lines, one line for each set of runs, all lines going through the origin. They are shown in Fig. 3, and their slopes directly measure the molecular second-order constant k_2'. In passing, we may note that equation (4) is the second-order rate-equation which so many of the earlier investigators thought they were observing (Part I, section 2), when in fact they were observing kinetics according to the other second-order equation (2), with the rate-constant k_2'' (Part II, section 2).

Molecular rate-constants are so constituted that they do not suffer change reflecting any effects of acidity on the acid–base equilibrium in which arylammonium and nitrite ions are involved. If these constants vary with acidity, then that means that the transition state, after the indicated amine and nitrous acid molecules have been supplied, requires

FIG. 3.

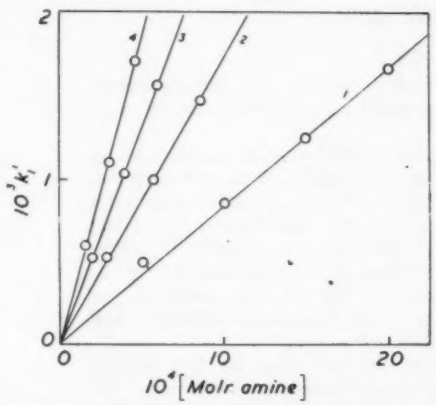


FIG. 4.

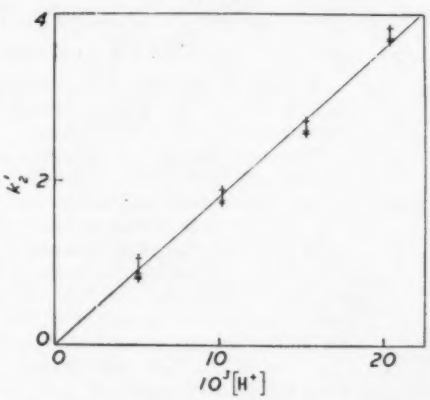


FIG. 3. *Diazotisation of* o*-chloroaniline: Plot of the molecular first-order rate-constant in nitrous acid* versus *the molecular concentration of amine. The different curves correspond to the different sets of runs, each set characterised by a different acidity. The hydrogen-ion concentrations are proportional to the figures used to number the sets, as noted beside the curves.*

FIG. 4. *Diazotisation of* o*-chloroaniline: Plot of the molecular second-order rate-constant* versus *the concentration of hydrogen ions.*

added or subtracted protons, wherefore the concentration of hydrogen ions appears to the appropriate positive or negative power in the complete kinetic equation. It is clear from Fig. 3 that the molecular second-order constants k_2' do vary with a positive power of the acidity; and indeed, if we plot the slopes of the curves against the hydrogen-ion concentration, we again get a straight line passing through the origin, as shown in Fig. 4. This establishes that one extra proton is required in the transition state of the reaction, and that the complete kinetic equation is (5):

$$\text{Rate} = k_3^{\text{H}}[\text{H}^+][\text{Ar}\cdot\text{NH}_2][\text{HNO}_2] \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

The rate-constant k_3^{H} of this third-order reaction of *o*-chloroaniline at 0° is 175 sec.$^{-1}$ mole^{-2} l.^{2}.

In Fig. 4, points are entered for the second-order constants of the individual runs, because the errors show a significant trend. Among the set of points belonging to each acidity, the highest point always corresponds to the lowest amine concentration. Also, the absolute spread of points is about the same at each acidity, and therefore it is proportionally greater at the lower acidities. In considering our experiments as illustrating equation (5), it has to be remembered that $[HNO_2]$ varies only during runs, whereas

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$[H^+]$ and [amine] are varied from run to run. Our errors suggest, then, that observed rates are raised above the rates required by equation (5), by a roughly constant amount, which makes a proportionally greater difference when [amine] is low, and, after that, when $[H^+]$ is low. This is just what would happen if the reaction according to equation (5) were not quite kinetically pure, but were accompanied by a small amount of reaction according to equation (2). This latter process does not kinetically depend either on [amine] or on $[H^+]$, and it is therefore not retarded, as reaction by equation (5) is retarded, when we cut down the concentrations of amine and hydrogen ions.

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17. *Nitrosation, Diazotisation, and Deamination. Part V.* Catalysis by Anions of Strong Acids in the Diazotisation of Aniline and of o-Chloroaniline in Dilute Perchloric Acid.*

By E. D. HUGHES and J. H. RIDD.

Perchlorate and nitrate ions do not catalyse diazotisation, and apparently fluoride ions do not, though chloride, bromide, and iodide ions do, with an importance increasing in this order.

The catalytic effect of chloride and bromide ions was first investigated by Schmid, who elucidated its kinetics as of first order each in hydrogen ion, amine, nitrous acid, and halide ion. We have tried so to adjust conditions that the reactions become of zeroth order in amine, whilst remaining of first order in each of the other reactants, by building up a sufficiently high concentration of a sufficiently reactive free-amine in the acid required by the catalysis. We failed for chloride-catalysis. For bromide-catalysis, we failed with aniline, but succeeded with the weaker base *o*-chloroaniline. And for iodide-catalysis we succeeded easily even with aniline.

It is shown that the process made rate-controlling in this way is completely independent of the process made rate-controlling when the kinetics of the uncatalysed reactions are similarly modified (Part II).

(1) *Survey of Anion Catalysis.*—The background against which we have to consider the catalysis of diazotisation by inorganic anions is that of two normally concurrent processes of diazotisation, the first uncatalysed and involving kinetics limited by the rate-laws (1) and (2), and the second catalysed by hydrogen ion and following the kinetic law (3):

$$\text{Uncatalysed}\begin{cases}\text{Rate} = k_3''[\text{Ar}\cdot\text{NH}_2][\text{HNO}_2]^2 & \ldots\ldots (1)\\ \text{Rate} = k_2''[\text{HNO}_2]^2 & \ldots\ldots (2)\end{cases}$$

$$\text{H}^+\text{-catalysed Rate} = k_3^{\text{H}}[\text{H}^+][\text{Ar}\cdot\text{NH}_2][\text{HNO}_2] \quad \ldots (3)$$

We have sought catalytic effects of added sodium perchlorate, nitrate, fluoride, chloride, bromide, and iodide. Up to concentrations of the order 0·1M, added sodium perchlorate and nitrate have no noticeable catalytic effect. This was expected for the perchlorate, because nitrosyl perchlorate does not exist in covalent form. But it could not have been confidently anticipated for the nitrate, since nitrosyl nitrate does exist in the form of dinitrogen tetroxide. However, this molecule seems to be a relatively poor nitrosating agent for primary aromatic amines (cf. Part I, section 1b). Fluoride appears to have no catalytic effect.

Added sodium chloride, bromide, and iodide exert catalytic effects, increasing in importance in this order, on the diazotisation of aniline or *o*-chloroaniline. This observation in itself is not new, because Schmid and Muhr [1] have described the catalytic effects

* Part IV, preceding paper.

[1] Schmid and Muhr, *Ber.*, 1937, **70**, 421; Schmid, *Z. Elektrochem.*, 1937, **43**, 626.

of chloride and bromide ion on the diazotisation of aniline, in the moderately strongly acid conditions in which the background rate for uncatalysed diazotisation is governed by equation (1). They showed that the kinetic effect of the halide ion is to add to the background rate a new rate-term of fourth order, as follows:

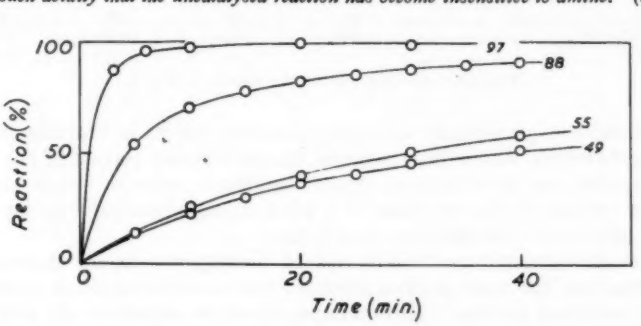
$$\text{Hal}^-\text{-Catalysed rate} = k_4^{\text{Hal}}[\text{H}^+][\text{Ar}\cdot\text{NH}_2][\text{HNO}_2][\text{Hal}^-] \quad . \quad . \quad . \quad (4)$$

Our object has been to discover whether equation (4) is really a limiting law, like equation (1). We had to try, either by cutting down the acidity, or by reducing the basicity of the amine, or by both devices, to break down the dependence of the catalytic rate on amine concentration, so carrying the kinetics, through a transitional situation, to another limiting form, possibly that of equation (5), which, analogously to equation (2), would represent the control of diazotisation rate by some purely inorganic process:

$$\text{Hal}^-\text{-Catalysed rate} = k_3^{\text{Hal}}[\text{H}^+][\text{HNO}_2][\text{Hal}^-] \quad . \quad . \quad . \quad . \quad (5)$$

So far, we have had no success in this attempt in the case of chloride-catalyses, but we have succeeded in that of bromide-catalyses, and more easily in that of iodide-catalyses.

FIG. 1. *Diazotisation of aniline. Runs illustrating bromide-catalysis, and its persistent dependence on amine, at such acidity that the uncatalysed reaction has become insensitive to amine.* (For details see Table 1.)



There can be no doubt that all these catalysed processes of diazotisation depend on preliminary inorganic-chemical reactions, which can be rate-controlling in principle, though in practice the conditions for such rate-control are not always easily fulfilled. The main condition is that a sufficient concentration of a sufficiently reactive amine shall be furnished in free-basic form to intercept completely the normal hydrolytic reversal of the formation in the preliminary process of the catalytic nitrosating agent. This condition becomes progressively easier to satisfy as we pass from chloride-, through bromide-, to iodide-catalysis.

(2) *Bromide-catalysis.*—Some experiments were first made in order to discover whether bromide-catalysis was to be thought of as an elaboration of the uncatalysed reaction, the basic kinetic form of which is comprised within equations (1) and (2). In this reaction, a preliminary, inorganic-chemical process occurs, which (we might suppose) bromide ions might extend to form a new nitrosating substance. Now the basic inorganic process becomes rate-controlling when acidity is so reduced that a concentration of free amine is built up which suffices to consume all the product of the process. When this happens, the kinetics change from those of equation (1) to those of equation (2). If the product of the same inorganic-chemical process were required for interaction with bromide ions in order to generate the active agent of bromide-catalysed diazotisation, then bromide-catalysis should disappear when the product of the basic process is wholly drawn off by amine, that is, when the uncatalysed kinetic form changes from that of equation (1) to that of

equation (2). We have shown that this does not happen; and we conclude that the bromide-catalysed reaction is not an elaboration of the uncatalysed reaction.

As evidence we may consider two pairs of runs on the diazotisation of aniline. They are specified as to conditions in Table 1, and compared as to results in Fig. 1. In all four runs, the initial concentration of nitrous acid is the same; and so is the concentration of free acid. The runs of the first pair are uncatalysed, whilst those of the second pair are catalysed by the same amount of sodium bromide. In the first run of each pair the initial concentration of aniline is the same; and in the second of each pair it is ten times greater than in the first. Now the acidity is at such a level that the uncatalysed reaction is proceeding essentially in accordance with equation (2). This is shown by the lower two curves in Fig. 1, which depict quite similar rates, though one run has ten times more amine than the other. The effect of bromide-catalysis is seen in the upper two curves in Fig. 1. They show that both the catalysed runs are greatly accelerated, and that the one with the larger amount of amine is much more accelerated than the other. Evidently, when the uncatalysed reaction goes over from kinetic form (1) to form (2), bromide-catalysis is preserved. Moreover, it is preserved in its amine-dependent kinetic form (4).

TABLE 1. *Bromide-catalysis in the diazotisation of aniline at low acidity at* 0°.

Initially added, $[HNO_2] = 0{\cdot}001$M, and [excess of $HClO_4$] = 0·002M, throughout.

Run	49	55	88	97
$[Ph{\cdot}NH_3^+ClO_4^-]$	0·001	0·01	0·001	0·01
[NaBr]	—	—	0·01	0·01

(The reaction–time curves are shown in Fig. 1.)

If, then, there is a preliminary inorganic-chemical process in bromide-catalysis, it is one which short-circuits, rather than extends, the preliminary process of the uncatalysed reaction: obviously, we have to go to greater lengths in order to isolate kinetically the suspected new process by the provision of a good organic-chemical trap for its product. This suggests recourse to a weaker base than aniline.

If the bromide-catalysed reaction is not to be regarded as an elaboration of the uncatalysed reaction, the most obvious alternative is to picture it as an extension of the hydrogen-ion catalysed process. The correspondences in equations (3) and (4) suggest this. Now the hydrogen-ion reaction of equation (3) was successfully investigated with *o*-chloroaniline as the diazotised amine (Part IV), and we therefore continued our study of bromide-catalysis in this example.

With *o*-chloroaniline as the diazotised amine, we can cut out the uncatalysed reaction of kinetic equations (1) and (2) practically completely by using very low concentrations of nitrous acid. When, as in these experiments, the initial stoicheiometric concentration of nitrous acid is 0·0001M, the only background reaction of which we have to take serious account is the hydrogen-ion reaction of equation (3). We know the rate of this at 0° (Part IV), and therefore we know what to subtract from diazotisation rates observed at 0° under bromide-catalysis, in order to isolate the catalytic rate term.

In all the runs now to be described, the amine was stoicheiometrically in large excess, and the acidity was large enough to remain substantially constant during a run. The bromide ions were not consumed. Thus the only concentration which was variable within a run was that of nitrous acid. By plotting the reaction–time curves in the usual semi-logarithmic way, it was found that the reaction including bromide-catalysis, just like the reaction without added bromide, was of first order in nitrous acid. This held for all the amine concentrations, acidities, and bromide concentrations investigated. A few examples are shown in Fig. 2.

From the slope of any such curve, we obtained a stoicheiometric, observed first-order rate-constant, $\bar{k}_1^{obs.}$. By the use of Table 3 of Part IV (or, in some cases, of an extension of such a Table), we can compute from this a molecular, observed, first-order rate-constant,

k_1^{obs}. This is the overall rate-constant of equation (6), which applies when the only variable concentration is that of nitrous acid:

$$\text{Rate} = k_1^{obs}[HNO_2] = (k_1' + k_1^{Br})[HNO_2] \quad . \quad . \quad . \quad . \quad . \quad (6)$$

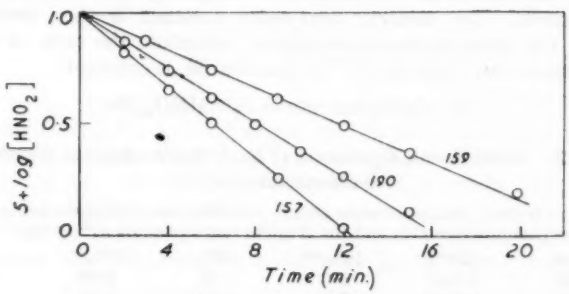
The rate-constant k_1^{obs} is the sum of a background constant k_1' and a catalytic constant k_1^{Br}. The background constant is the product of certain factors taken from equation (3), as follows:

$$k_1' = k_3^{H}[H^+][Ar{\cdot}NH_2] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

From Part IV, section 3, we know that, for *o*-chloroaniline at 0°, k_3^{H} is 175 sec.$^{-1}$ mole^{-2} l.^{2}. Hence, from this figure, the hydrogen-ion concentration applying to the run, and the concentration of stoicheiometric amine, in constant excess, during the run, together with the proportion in which the amine is present in molecular form, as given by Table 3 of Part IV, or a similar Table, we can compute the background first-order rate-constant k_1'. Thus we may obtain the catalytic first-order rate-constant, k_1^{Br} by subtraction of k_1' from the observed constant k_1^{obs}.

Now we know that the background rate-constant k_1' depends on the amine concentration, as in equation (7), and the point to be determined is whether the catalytic

FIG. 2. *Diazotisation of o-chloroaniline in the presence of bromide ions. Plot of the logarithm of the concentration of nitrous acid* versus *the time, for various constant concentrations of amine, hydrogen ion, and bromide ion* (*cf. Tables* 2—4).



rate-constant k_1^{Br} similarly depends on the concentration of the amine, or whether, by a sufficient raising of the concentration of free-basic amine, this constant has been, or can be, made independent of that concentration. At a fixed acidity, the molecular amine concentration is a constant fraction of the stoicheiometric amine concentration. Several runs at a common fixed acidity, but with a range of concentrations of stoicheiometric amine in constant excess, are cited in Table 2, where the observed, molecular first-order rate-constants,

TABLE 2. *Bromide-catalysed diazotisation of o-chloroaniline with a low concentration of nitrous acid at* 0°. *Effect of amine concentration on the background and catalytic rates.*

Initially, $[H^+] = 0{\cdot}0051$, $[Br^-] = 0{\cdot}0004$, and [stoicheiometric HNO_2] = 0·0001M. All rate-constants in sec.$^{-1}$.

Run	[Stoich. amine]	$10^3k_1^{obs}$	$10^3k_1'$	$10^3k_1^{Br}$
156	0·001	2·05	0·22	1·83
155	0·002	2·65	0·43	2·22
163	0·003	2·97	0·65	2·31
157	0·004	3·33	0·87	2·46

k_1^{obs}, are split up, by the method described above, into their background and catalytic components, k_1' and k_1^{Br}. One sees that, when the amine concentration is high enough,

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the catalytic rate-constant k_1^{Br} is almost independent of it. Thus, when the stoicheiometric amine concentration is doubled, between 0·001M and 0·002M, the catalytic constant is raised by only 20%; and when the concentration is again doubled, between 0·002M and 0·004M, the constant is raised further by only 10%. At higher concentrations the rates become somewhat too great for accurate measurement, because the background rate continues to go up, even though the catalytic rate does not. However, there can be no doubt that, even over the concentration range explored, the catalytic rate is substantially of zeroth order in amine.

The summary of this finding is that, whilst the background term in equation (6) is under the restriction that the only variable concentration shall be that of nitrous acid, the catalytic term holds when the concentrations of nitrous acid and amine are both variable. It is therefore convenient to break up equation (6), and consider further only the catalytic part, now rewritten as equation (8):

$$Br^-\text{-Catalysed rate} = k_1^{Br}[HNO_2] \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

The remaining problem is to determine how k_1^{Br} depends on the other two possibly variable concentrations, those of bromide ions and of hydrogen ions, when the concentration of free amine is large enough not to appear in the rate equation.

The answer with respect to bromide-ion concentration is contained in Table 3, which records rate-constants for a series of runs, all with a sufficiently high concentration of amine, and with a fixed acidity, but with various concentrations of bromide ion. The observed, molecular, first-order rate-constants are split up as before into their background and catalytic parts. The catalytic first-order constant is then seen to be directly proportional to the bromide-ion concentration, wherefore the ratio of these quantities, which is the second-order constant k_2^{Br} of equation (9), is constant:

$$Br^-\text{-Catalysed rate} = k_2^{Br}[HNO_2][Br^-] \quad . \quad . \quad . \quad . \quad . \quad (9)$$

TABLE 3. *Bromide-ion dependence of the bromide-catalysed diazotisation of o-chloroaniline at* 0°.

Initially, $[H^+] = 0·0051$, [stoicheiometric amine] = 0·0040, and [stoicheiometric HNO_2] = 0·0001M. All first-order rate-constants in sec.$^{-1}$, and the second-order constants k_2^{Br} in sec.$^{-1}$ mole^{-1} l.

Run	$[Br^-]$	$10^3k_1^{obs}$	$10^3k_1'$	$10^3k_1^{Br}$	k_2^{Br}
188	0·0001	1·47	0·87	0·60	6·00
189	0·0002	2·08	0·87	1·21	6·05
190	0·0003	2·63	0·87	1·76	5·87
157	0·0004	3·33	0·87	2·46	6·15

TABLE 4. *Hydrogen-ion dependence of the bromide-catalysed diazotisation of o-chloroaniline at* 0°.

Initially, [stoicheiometric HNO_2] = 0·0001M, throughout; k_1^{obs} and k_1^{Br} are in sec.$^{-1}$, k_2^{Br} is in sec.$^{-1}$ mole^{-1} l., and k_2^{Br} is in sec.$^{-1}$ mole^{-2} l.^{2}.

Run	$[H^+]$	[Stoich. amine]	$[Br^-]$	$10^3k_1^{obs}$	$10^3k_1'$	$10^3k_1^{Br}$	k_2^{Br}	$10^{-3}k_2^{Br}$
158	0·0017	0·002	0·0010	2·28	0·28	2·00	2·00	1·18
159	,,	0·001	,,	2·13	0·15	1·98	1·98	1·17
160	0·0034	0·003	0·0004	2·17	0·58	1·58	3·95	1·16
161	,,	0·002	,,	1·97	0·38	1·58	3·95	1·16
157	0·0051	0·004	,,	2·33	0·87	2·46	6·15	1·21
163	,,	0·003	,,	2·97	0·65	2·31	5·78	1·13
190	,,	0·004	0·0003	2·63	0·87	1·76	5·87	1·15
189	,,	,,	0·0002	2·08	0·87	1·21	6·05	1·19
188	,,	,,	0·0001	1·47	0·87	0·60	6·00	1·18

The final question is that of the dependence of the second-order catalytic constants k_2^{Br} on acidity. To settle this, several sets of runs were done, each set characterised by a different acidity. The results are in Table 4. From them, we see that the second-order catalytic constants are directly proportional to the hydrogen-ion concentration. It follows

that the full kinetic equation for the catalysed reaction is the third-order equation (10), the rate-constant of which, as the last column of the Table shows, remains constant under variations in the concentrations of all substances involved in the reaction:

$$Br^-\text{-Catalysed rate} = k_3^{Br}[H^+][HNO_2][Br^-] \quad . \quad . \quad . \quad . \quad (10)$$

The mean rate-constant, k_3^{Br}, at 0° is 1170 sec.$^{-1}$ mole^{-2} l.^{2}.

Equation (10) is a specialised form of equation (5). It is the kinetic equation of a purely inorganic-chemical process, preliminary to bromide-catalysed diazotisation, and of such a nature that it can become rate-controlling. When the amine draws off the product of this first process much more slowly than the process itself becomes reversed, then the catalytic reaction has the kinetic form observed by Schmid and Muhr, and represented by equation (4). But when a sufficiently reactive amine is supplied in sufficient concentration as free base wholly to trap the product of the preliminary process, then the catalytic rate ceases to depend on the amine, and so the kinetics become simplified to those of equation (5). As will be shown in Part VI, a kinetic transition such as this fully establishes the chemical mechanism.

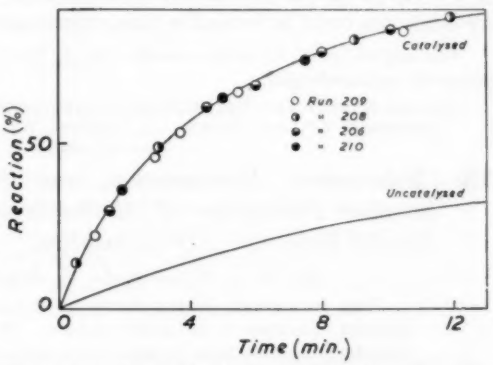

FIG. 3. *Diazotisation of aniline. Runs illustrating iodide-catalysis, and its independence of amine at such acidity that the uncatalysed reaction is also insensitive to amine.*
The lower curve represents an uncatalysed run. The upper curve is common to a series of runs, catalysed with the same concentration of iodide ion, but differing with respect to amine concentration over a 23-fold range.

The data of Table 4 leave no room for a bromide-catalysed rate term which does not depend on hydrogen ions; and nowhere in this work has any sign of such a rate-term been encountered.

(3) *Iodide-catalyses.*—The transition of kinetic form, in which the factor dependent on amine disappears from the rate equation, is much easier to observe with the iodide-catalysis of diazotisation than with its bromide-catalysis. It is not necessary to resort to the diazotisation of any weaker base than aniline in order to demonstrate this effect in iodide-catalysis. If the diazotisation of aniline in aqueous perchloric acid, with such a concentration of nitrous acid that the uncatalysed reaction is almost the only background process, is followed at progressively reduced acidities, then, even before the transition from kinetic form (1) to form (2) in the background process is complete, the transition from form (4) to form (5) in a superposed iodide-catalysed reaction is quite complete. The total rate is now essentially independent of the amine, and is expressed by equation (11):

$$\text{Rate} = k_2''[HNO_2]^2 + k_3^I[H^+][HNO_2][I^-] \quad . \quad . \quad . \quad . \quad . \quad (11)$$

Details are given in support of the main conclusion here summarised by citation of the series of runs specified as to conditions in Table 5, and compared as to results in Fig. 3. All these runs were started with a common stoicheiometric concentration of nitrous acid and a common acidity. An uncatalysed run is included as a standard of reference: it is a close reproduction of some of the second-order runs recorded in Part II. All the other runs of the set are catalysed by the same concentration of sodium iodide. They differ widely with respect to concentration of amine, and yet the kinetic course of all these runs

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TABLE 5. *Iodide-catalysis in the diazotisation of aniline at low acidity at* 0°.

Initially, [stoicheiometric HNO_2] = 0·001, and [excess of $HClO_4$] = 0·002M, throughout.

Run	201	209	208	206	210
$[Ph{\cdot}NH_3^+ClO_4^-]$	0·010	0·001	0·005	0·010	0·023
[NaI]	—	0·001	0·001	0·001	0·001

(The reaction-time curves are shown in Fig. 3.)

is described by a common curve. Further analysis of such runs shows them to be consistent with equation (11). The third-order rate-constant k_3^I has the value 1370 sec.$^{-1}$ mole^{-2} l.^{2}. This is evidently the rate-constant of a preliminary inorganic-chemical process, which, at the low acidities used in these measurements, is rate-controlling for iodide-catalysed diazotisation.

It may be noted that the iodide-catalysed diazotisations went to completion as accurately as did the uncatalysed diazotisations. Thus, no decomposition of nitrous acid by iodide ions could be noticed in these experiments.

The help of Dr. K. G. Oldham and of Dr. J. Wilby in making some of these measurements is gratefully acknowledged.

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18. *Nitrosation, Diazotisation, and Deamination. Part VI.* Comparative Discussion of Mechanisms of* N- *and* O-*Nitrosation with Special Reference to Diazotisation.*

By E. D. HUGHES, C. K. INGOLD, and J. H. RIDD.

The six discrete kinetic forms in which aqueous diazotisation has been studied diagnose a net-work (scheme 20, p. 95) of inorganic-chemical transformations which produce, and may interconvert, various nitrosation carriers, any of which may nitrosate the amine. Apart from the common basic step of conversion of nitrous acid into its conjugate acid, any one of the steps of production, or interconversion, of the nitrosating agents, or of the attack of any of them on the amine, may be made rate-controlling, the overall kinetics changing accordingly. No step after that which first implicates the amine ever becomes rate-controlling.

In weakly acidic aqueous media, the important carriers are nitrous acidium ion, dinitrogen trioxide, and nitrosyl chloride, bromide, and iodide, but not nitrosonium ion, dinitrogen tetroxide, nitrosyl carboxylates, or nitrous acid. Nitrosonium ions are not produced, and nitrous acid is present but useless. Nitrosyl carboxylates nitrosate nitrite ion more easily than they nitrosate amines, and thus they catalyse nitrosation of the latter by way of dinitrogen trioxide.

Recent literature on the kinetics of *N*- and *O*-nitrosation is reviewed, and some discrepancies are explained. Okano and Ogata's claim for $HN_2O_3^+$ as a main nitrosating agent in aqueous diazotisation arises from their not controlling kinetic form before calculating rate-constants. Most other difficulties can be traced to the fallacy that buffers do nothing except control pH. Dusenbury and Powell's discrepant results for deamination arise, as was previously pointed out, from unrecognised catalysis by their phosphate buffer, which produces the nitrosating species NOH_2PO_4 and $NOHPO_4^-$. Anbar and Taube's similarly discrepant results for the nitrosation of water, as followed by oxygen exchange, arise from the same cause. Other modern work is cited which agrees well with that now recorded.

(1) KINETICS AND MECHANISMS OF DIAZOTISATION

(a) *The Kinetic Forms of Diazotisation.*—The immediately preceding four papers have dealt with diazotisation in a number of discrete kinetic forms, which it is convenient here

* Part V, preceding paper.

to bring together. Our convention is again so to write kinetic equations that the entries in brackets are to be given a literal (molecular or ionic) rather than an analytical (stoicheiometric) interpretation; in other words, acids and bases are expressed with exclusion of their conjugate bases and conjugate acids, respectively:

(*a*) *Uncatalysed diazotisation* (cf. Parts II and III):

$$\begin{cases} \text{Rate} = k_3''[\text{amine}][\text{HNO}_2]^2 & \ldots\ldots\ldots (1) \\ \text{Rate} = k_2''[\text{HNO}_2]^2 & \ldots\ldots\ldots (2) \end{cases}$$

(*b*) *Carboxylate-ion catalysed diazotisation* (cf. Part III):

$$\text{Rate} = k_3^{\text{OAc}}[\text{HNO}_2]^2[\text{OAc}^-] \quad \ldots\ldots\ldots (3)$$

(*c*) *Hydrogen-ion catalysed diazotisation* (cf. Part IV):

$$\text{Rate} = k_3^{\text{H}}[\text{amine}][\text{H}^+][\text{HNO}_2] \quad \ldots\ldots\ldots (4)$$

(*d*) *Halide-ion catalysed diazotisation* (cf. Part V):

$$\begin{cases} \text{Rate} = k_4^{\text{Hal}}[\text{amine}][\text{H}^+][\text{HNO}_2][\text{Hal}^-] & \ldots\ldots\ldots (5) \\ \text{Rate} = k_3^{\text{Hal}}[\text{H}^+][\text{HNO}_2][\text{Hal}^-] & \ldots\ldots\ldots (6) \end{cases}$$

The brace between equations (1) and (2) is a reminder that they are limiting equations. Each alone has a great range of validity, but they enclose between them a band of continuously transitional kinetic forms. In order to accomplish, with a given amine, the transition from limit (1) to limit (2), it is necessary to raise sufficiently the concentration of free-basic amine: the diazotisation rate will then at first rise proportionally, according to equation (1), then less steeply, and finally not at all as a maximum rate is reached, which is given by equation (2).

Similarly, equations (5) and (6) are limiting equations, which bracket a band of transitional kinetic forms; and the conditions for securing a transition from equation (5) to equation (6) are essentially the same as has just been described for the transition from equation (1) to equation (2).

(b) *Uncatalysed Diazotisation.*—The experimental proof that kinetic forms (1) and (2) are both valid, and that a transition from form (1) to form (2) can be produced by raising the supply of molecular amine, completely proves the reaction mechanism. The argument is as follows.

In the first place, the finding shows that there can be no slow step after that step in which the amine is implicated: if there were, we could never get rid of the amine factor from the kinetic equation. That is to say, we have established the conclusion, set down in anticipation in Part I, section 1a, that rate control is complete when primary nitrosation is complete, and that none of the changes undergone by the immediate nitrosation product, or by species formed from it, as set out in outline schemes (1) and (2) of Part I, section 1a, has any influence on the kinetics. It is a part of this conclusion that all kinetic interpretations on the lines of general acid and general base catalysis, explanations of the type of which, as mentioned in Part I, section 2, Kenner's suggestion is an example, are excluded. For it is essential to such interpretations that they contain a slow step of proton transfer subsequent to the nitrosating step.

The next conclusion to which the observation of the kinetic transition gives rise is that the process leading to primary nitrosation itself consists of more than one step. For only a last step in any such sequence can involve the amine, and the kinetic transition shows that, whilst that step may be rate-controlling, when, in this situation, we increase its speed by feeding more amine, some earlier step not involving amine will eventually become the bottle-neck. In other words, some inorganic-chemical process, which is slow enough to be rate-controlling, when other rate restrictions are removed, must first produce the nitrosation carrier. Then this can attack the amine.

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Reference to Part I, section 1c, and particularly to equations (5)—(11) of that section, will show that the nitrosation carrier can be nothing else than dinitrogen trioxide. That carrier should lead to the two limiting kinetic forms (1) and (2), and to a kinetic transition from form (1) to form (2) under a sufficiently free supply of molecular amine. This prediction has been verified in its entirety.

The kinetic equation for the preliminary self-dehydration of nitrous acid to form dinitrogen trioxide is equation (2), and we measure this inorganic-chemical process when we follow diazotisation kinetics in the form of equation (2).

The most plausible scheme for the self-dehydration, though its actual support is only that of analogy with reactions of nitrous acid discussed later, is the scheme of equations (7), which assumes slow attack by the nitrite ion on the conjugate acid of nitrous acid:

$$\left.\begin{aligned} HNO_2 &\underset{\text{Fast}}{\rightleftharpoons} H^+ + NO_2^- \\ H^+ + HNO_2 &\underset{\text{Fast}}{\rightleftharpoons} H_2NO_2^+ \\ O_2N^- + NO{-}OH_2^+ &\underset{\text{Slow}}{\rightleftharpoons} O_2N{-}NO + OH_2 \end{aligned}\right\} \quad . \quad . \quad . \quad . \quad . \quad (7)$$

The slow step here might be a strictly one-stage, bimolecular, nucleophilic substitution S_N2, or it might involve an additive intermediate of low stability, such as Bender first demonstrated for reactions of substitution in the carboxyl group.

The rate-equation (2) applies to the combined three steps of scheme (7). The rate-constant k_2'' for the formation of dinitrogen trioxide, at 0° in water, from two molecules of nitrous acid according to this equation is 0·85 sec.$^{-1}$ mole^{-1} l., according to the experiments of Part II in perchloric acid at low ionic strength, or is 0·78 sec.$^{-1}$ mole^{-1} l., according to the work of Part III in buffers at the ionic strength 0·1M. For comparison with carrier-forming reactions considered later, it is convenient to write a kinetic equation for the combined second and third steps of scheme 7: this is equation (8):

$$\text{Rate} = k_3^{\text{Nit}}[H^+][HNO_2][NO_2^-] \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

The rate-constant of this equation, k_3^{Nit}, represents the rate of attack of supplied nitrite ion on pre-equilibria nitrous acidium ion. It differs from k_2'' by the factor of the acidity constant of nitrous acid, which we take as $4{\cdot}5 \times 10^{-4}$ mole l.$^{-1}$. The values of k_3^{Nit} are 1890 sec.$^{-1}$ mole^{-2} l.^{2}, according to the experiments of Part II, or 1740 sec.$^{-1}$ mole^{-2} l.^{2}, according to those of Part III.

When the supply of molecular amine is sufficiently restricted, the last step of scheme (7) becomes fast in comparison with the first of scheme (9):

$$\left.\begin{aligned} Ar{\cdot}NH_2 + NO{\cdot}NO_2 &\xrightarrow[\text{Slow}]{} Ar{\cdot}NH_2{\cdot}NO^+ + NO_2^- \\ Ar{\cdot}NH_2{\cdot}NO^+ &\xrightarrow[\text{fast steps}]{\text{Several}} Ar{\cdot}N_2^+ + H_2O \end{aligned}\right\} \quad . \quad . \quad . \quad (9)$$

The kinetic equation is now equation (1), which we can, if we choose, rewrite in form (10). Equations (10) and (8) are then in the same forms as equations (5) and (6), respectively.

$$\text{Rate} = k_4^{\text{Nit}}[\text{amine}][H^+][HNO_2][NO_2^-] \quad . \quad . \quad . \quad . \quad . \quad (10)$$

(c) *Carboxylate-ion Catalysed Diazotisation.*—The rate-equation (3) shows that the measured process is one of the formation of a nitrosation carrier, which is taken up by the amine as fast as it is produced. It also shows that two molecules of nitrous acid, plus one of the carboxylate ion, plus or minus undetermined water molecules, are required to build the transition state of the process which leads to the carrier.

There are only two possibilities for producing such a transition state. Either,

dinitrogen trioxide is formed in pre-equilibrium, and is then converted in a rate-controlling way into the acyl nitrite, which becomes the effective nitrosating agent:

$$\left.\begin{aligned} NO_2^- + NO{\cdot}OH_2^+ &\underset{\text{Fast}}{\rightleftharpoons} NO_2{\cdot}NO + OH_2 \\ AcO^- + NO{\cdot}NO_2 &\xrightarrow[\text{Slow}]{} AcO{\cdot}NO + NO_2^- \end{aligned}\right\} \quad . \quad . \quad . \quad . \quad (11)$$

Or, the acyl nitrite is formed in pre-equilibrium, and is then converted in a rate-controlling manner into dinitrogen trioxide, which is still the nitrosating agent, just as in the uncatalysed reaction:

$$\left.\begin{aligned} AcO^- + NO{\cdot}OH_2^+ &\underset{\text{Fast}}{\rightleftharpoons} AcO{\cdot}NO + OH_2 \\ NO_2^- + NO{\cdot}OAc &\xrightarrow[\text{Slow}]{} NO_2{\cdot}NO + OAc^- \end{aligned}\right\} \quad . \quad . \quad . \quad . \quad (12)$$

Of the two schemes (11) and (12), both consistent with the kinetic form, only (12) can lead to catalysis. Supposing diazotisation, in the absence of carboxylate ions, to be proceeding at its maximum uncatalysed rate, that which is given by the amine-independent equation (2), then, since, under scheme (11), carboxylate ions could only intercalate a step which is slower than the one which was the slowest before, they could not divert any dinitrogen trioxide from direct uptake by the amine; and therefore they could have no kinetic effect, not even a retarding one. On the other hand, the carboxylate ions could be accelerating under scheme (12), because they would then provide a new, and possibly faster, route for the formation of dinitrogen trioxide.

We conclude that this is essentially how carboxylate ions do act: they catalyse the formation of the original nitrosation carrier: they do not change the carrier. That was part of the value to us of carboxylate buffers in the experiments recorded in Part III: many buffers would just as adequately have controlled the pH; but some at least would have changed the nitrosating agent.

The kinetics of scheme (12) are expressed by equation (13), which is, of course, equivalent to equation (3):

$$\text{Rate} = k_4^{OAc}[OAc^-][H^+][HNO_2][NO_2^-] \quad . \quad . \quad . \quad . \quad . \quad (13)$$

The rate constant k_4^{OAc}, calculated with $4{\cdot}5 \times 10^{-4}$ mole $l.^{-1}$ as the value of the acidity constant of nitrous acid, is 85,000 $sec.^{-1}$ $mole^{-3}$ $l.^3$ for acetate ions, and 360,000 $sec.^{-1}$ $mole^{-3}$ $l.^3$ for phthalate ions.

(d) *Hydrogen-ion Catalysed Diazotisation* (*Introduction*).—The kinetic equation (4) shows that a cationic nitrous species is being formed in some relatively rapid pre-equilibrium, and is then nitrosating the amine in a rate-controlling fashion. Reference to Part I, section 1c, and particularly to the set of equations (5)—(11) in that section, will show that two carriers could account for the observed kinetics. They are the nitrous acidium ion and the nitrosonium ion.

The relation between these alternative carriers is the same as that between the nitric acidium ion and the nitronium ion in nitration, and between the hypochlorous acidium ion and the chlorinium ion in chlorination. The nitrous acidium ion is the product of a pre-equilibrium process (14), which is inevitably rapid, whilst the nitrosonium ion is formed from the acidium ion by a heterolytic bond-fission (15), which is in principle slow, and could conceivably be made rate-controlling—just as the analogous formation of the nitronium ion, and that of the chlorinium ion, have in fact been made rate-controlling in nitration and chlorination, respectively:

$$H^+ + HNO_2 \underset{\text{Fast}}{\rightleftharpoons} H_2NO_2^+ \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (14)$$

$$ON{-}\overset{\curvearrowright}{\overset{+}{O}}H_2 \underset{\text{Slow}}{\rightleftharpoons} NO^+ + OH_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad (15)$$

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If the cationic nitrosation carrier is indeed the nitrous acidium ion, then the kinetic equation is, universally, equation (4). If, however, the carrier is the nitrosonium ion, then kinetics of form (4) might still be observed, but now only as a limit, a change to kinetic form (16), in which the rate becomes independent of amine concentration, being in principle possible:

$$\text{Rate} = k_2^{\text{H}}[\text{H}^+][\text{HNO}_2] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (16)$$

If we can observe such a kinetic change, we establish the nitrosonium ion as carrier unambiguously. In order to make the observation we must intercept the reversal of process (15), by the efficient trapping of nitrosonium ion with amine, so making the forward process (15) rate-controlling. We tried to do this, but could see no sign of a change from kinetic form (4) to form (16). At this point, then, we were left with an ambiguous conclusion: either the carrier is the nitrous acidium ion, and our kinetic observation is already complete; or it is the nitrosonium ion, but our trapping system was not efficient enough to prove it.

When such ambiguities arise, it is a good general rule to introduce mechanistic competition, even though this involves making the system more complicated. That was why we took up the study of halide-ion catalysis. We shall consider that subject next, and then return to close the gap in the present argument.

(e) *Halide-ion Catalysed Diazotisation.*—Fluoride-ion catalysis seems not to occur. In catalysis by the other halide ions, we observe, overall, both the limiting kinetic forms (5) and (6), though there is a distinction between the cases, in that form (6) could not be observed with chloride ion, but was particularly easily observed with iodide ion.

The first conclusion to be drawn from the observation of kinetic form (6) is that halide ions are not participating in general-acid–general-base catalysis. By an argument similar to one used in sub-section (1b), we can show that no element of rate-control enters later than the step of attack on the amine.

Again, by an argument similar to another of those employed in sub-section (1b), we can show that primary nitrosation of the amine is itself the result of a succession of steps. First, a purely inorganic-chemical process produces the nitrosating agent; then this attacks the amine; and, according to the conditions, either of these steps may become rate-controlling.

The rate of the inorganic-chemical carrier-forming process is that which is measured as diazotisation rate in the form of equation (6). This equation unambiguously identified the carrier as the nitrosyl halide.

Equation (6) represents a nucleophilic substitution by supplied halide ion in pre-equilibrium nitrous acidium ion. This process, represented in scheme (17), is completely analogous to the second and third steps of scheme (7), for the formation of dinitrogen trioxide:

$$\left.\begin{aligned} \text{H}^+ + \text{HNO}_2 &\underset{\text{Fast}}{\rightleftharpoons} \text{H}_2\text{NO}_2^+ \\ \text{Hal}^- + \text{NO–OH}_2^+ &\underset{\text{Slow}}{\rightleftharpoons} \text{Hal–NO} + \text{OH}_2 \end{aligned}\right\} \quad . \quad . \quad . \quad . \quad (17)$$

Correspondingly, the kinetic equation (6) for the formation of nitrosyl halides is analogous to kinetic equation (8) for the formation of dinitrogen trioxide.

It is of interest to compare our rate-constants, k_3^{Hal} and k_3^{Nit}, of formation of nitrosyl halides and dinitrogen trioxide (nitrosyl nitrite) from supplied halide or nitrite ion and pre-equilibrium nitrous acidium ion. The values for 0° in water are as follows:

$$\text{NOBr, 1170; NOI, 1370; } \text{NONO}_2\text{, 1890 (sec.}^{-1}\text{ mole}^{-2}\text{ l.}^2\text{)}$$

(f) *Hydrogen-ion Catalysed Diazotisation (Conclusion).*—There is another way, than that of the second step of scheme (17), through which a nitrosyl halide could, and certainly would, be formed, were nitrosonium ion available, *viz.*, through the simple ionic association (18):

$$\text{Hal}^- + \text{NO}^+ \longrightarrow \text{Hal·NO} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (18)$$

No bond is broken in this process, which would therefore be fast, indeed, for practical purposes, instantaneous.

By measurements of diazotisation in accordance with the kinetic equation (6), we have found the rates of formation of nitrosyl bromide and iodide. Apart from a reservation mentioned below, these observed rates will be upper limits to any possible rate at which nitrosonium ion could appear in the solutions under the conditions of the measurements.

At the end of sub-section (1d), the mechanism of hydrogen-ion catalysed diazotisation was left unsettled, insofar as the nitrosation carrier might be nitrous acidium ion or nitrosonium ion. We can now carry the matter further. For, as described in Part V, we have run two processes of diazotisation of *o*-chloroaniline in competition, *viz.*, diazotisation under hydrogen-ion catalysis, and under bromide-ion catalysis. The rates of the concurrent reactions were compared. Moreover, the bromide-ion reaction, for its part, was run under such conditions that its rate was the rate of formation of nitrosyl bromide, and therefore, according to the suggestion in the preceding paragraph, an upper limit to any possible rate of appearance of nitrosonium ion. Therefore, if the hydrogen-ion reaction were to depend on nitrosonium ion, it could never go faster than the bromide-ion reaction. But, in fact, the rate laws show that the two reactions are not kinetically tied together, and that the rates themselves can stand in either order. Each rate follows its own kinetic law, the hydrogen-ion rate increasing proportionally to amine, but not bromide, concentration, and the bromide-ion reaction proportionally to bromide, but not amine, concentration. If the amine concentration is high enough, and the bromide concentration low enough, the hydrogen-ion reaction will go faster than the bromide-ion reaction (cf. for example, Part V, Table 4, Run 188). The inference is that the hydrogen-ion reaction does not involve the nitrosonium ion, and that, therefore, its carrier must be the nitrous acidium ion.

We must deal with an apparent loop-hole in this argument. This is as follows. We can admit that the combination of formed nitrosonium ion with bromide ion would be practically instantaneous; but we might assume that its combination with all bond-forming nucleophiles, even the neutral ones, amine and water, is also practically instantaneous. Then, in order to account for the mutual independence of the kinetics of the hydrogen-ion and bromide-ion reactions, we should have to assume that the recombination of formed nitrosonium ion with water is its most immediate reaction of all, so that amine and bromide ion are able, additively and independently, to " tap off " nitrosonium ion from a fully maintained stationary concentration. In other words, we must assume that nearly all the nitrosonium ion, primarily formed from nitrous acidium ion, goes back into nitrous acidium ion, and that only very small fractions of it are caught by amine and by bromide ion. In still other words, we must assume that the rate of the primary dehydration of nitrous acidium ion to nitrosonium ion is almost equal to the rate of rehydration of the latter, and is thus very much greater than either of the measured rates of diazotisation, and, in particular, very much greater than that measured rate which is identified with the rate of formation of nitosyl bromide. This has further implications. It was shown in sub-section (1e) that the rates of formation of nitrosyl bromide, nitrosyl iodide, and dinitrogen trioxide are all the same to well within a factor of 2. Therefore the assumption, to which we are forced, when we try to get over the difficulty of making the nitrosonium ion an intermediate in hydrogen-ion catalysed diazotisation by adopting it as an extra intermediate in halide-catalysed, and, as would then follow, in all forms of diazotisation, includes the particular assumption that the rate of the primary dehydration of nitrous acidium ion to nitrosonium ion is very much greater than the second-order rate of self-dehydration of nitrous acid to dinitrogen trioxide. Now we know the latter rate: it is the upper limiting rate of uncatalysed diazotisation in weakly acidic aqueous conditions. We also know—for this has been shown by Bunton, Llewellyn, and Stedman, as will be noted in sub-section (2c)—that, in such conditions, there is no faster mechanism

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for oxygen exchange between nitrous acid and water than that of the second-order self-dehydration of nitrous acid to dinitrogen trioxide. Therefore the assumption, to which our attempt to drag the nitrosonium ion into the picture has led us, that of a very fast, reversible, acidic dehydration of nitrous acid to nitrosonium ion, necessarily much faster than the limiting rate of uncatalysed diazotisation, is false. Thus the apparent loop-hole in the previous argument is unreal.

Our final conclusion is, then, that the nitrous acidium ion, not the nitrosonium ion, is the carrier in hydrogen-ion catalysed diazotisation. It has also emerged in the discussion that the nitrosonium ion does not intervene in any of the forms in which diazotisation has been observed to take place in weakly acid solution. It follows that the nitrous acidium ion substitutes, whether by organic or inorganic, and whether by anionic or molecular, nucleophiles, always by an S_N2 mechanism, and never by an S_N1 mechanism, in the range of conditions which our investigation covers.

It follows from this interpretation that, in the study of the hydrogen-ion reaction described in Part IV, we were measuring the rate of attack of supplied *o*-chloroaniline on pre-equilibrium nitrous acidium ion:

$$\left.\begin{array}{l} H^+ + HNO_2 \underset{\text{Fast}}{\rightleftharpoons} H_2NO_2^+ \\ o\text{-}Cl\cdot C_6H_4\cdot NH_2 + NO{-}OH_2^+ \xrightarrow[\text{Slow}]{} o\text{-}Cl\cdot C_6H_4\cdot NH_2\cdot NO^+ + OH_2 \\ o\text{-}Cl\cdot C_6H_4\cdot NH_2\cdot NO^+ \xrightarrow[\text{fast steps}]{\text{Several}} o\text{-}Cl\cdot C_6H_4\cdot N_2^+ + H_2O \end{array}\right\} \quad . \quad (19)$$

The first two steps of scheme (19) are exactly like scheme (17), and like the last two steps of scheme (7), except that a neutral, rather than an anionic, nucleophile is attacking the nitrous acidium ion. The overall rate-constant k_3^H of process (19) is 175 sec.$^{-1}$ mole^{-2} l.^{2}, a figure to be compared with those given at the end of the preceding sub-section.

As we do not know the acidity constant of the nitrous acidium ion, we cannot give absolute values for the rates of substitution in it of the various nucleophiles considered. The relative values of these rates are as follows:

$$o\text{-}Cl\cdot C_6H_4\cdot NH_2,\ 1;\ Br^-,\ 6{\cdot}7;\ I^-,\ 7{\cdot}8;\ NO_2^-,\ 10{\cdot}8$$

(g) *The Mechanisms of Diazotisation.*—Our investigation of diazotisation has been confined to weakly acidic aqueous media. Of the possible carriers of the nitrosation process, which were listed for consideration in Part I, section 1b, the following have been found effective in these conditions:

$$H_2NO_2^+ \qquad NOI \qquad NOBr \qquad NOCl \qquad N_2O_3$$

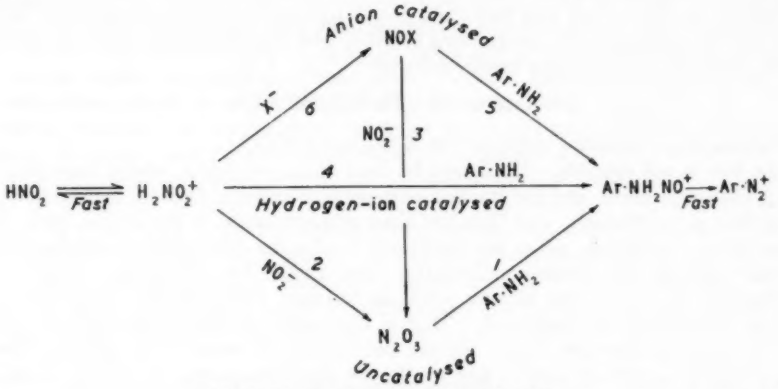
The following possible carriers have been found to be much less effective, or ineffective, *viz.*,

$$NO^+ \qquad N_2O_4 \qquad NO_2Ac \qquad NO_2H$$

though this may be either because, as in the case of NO^+, they are not formed in the conditions, or because, as with NO_2H, they are formed, but are useless as direct nitrosating agents.

The mechanisms by which the effective carriers act are not all independent. The first step of all of them is the formation of the nitrous acidium ion. In this ion, a water molecule is holding the place that has eventually to be taken by the amine molecule. The amine molecule may substitute itself for water directly, and so become nitrosated. This is hydrogen-ion catalysed diazotisation. Alternatively, an anion may first displace the water, and become itself subsequently displaced by the amine, which thus becomes nitrosated. In the special case in which the substituting anion is nitrite ion, the intermediate product is dinitrogen trioxide, which is now the nitrosating agent towards the amine. This is uncatalysed diazotisation. In the general case in which some other anion

first substitutes and then becomes displaced, the intermediate is a general nitrosyl compound, which nitrosates the amine. We call this anion-catalysed diazotisation. If a general anion introduces itself, and is then displaced by nitrite ion, which is finally displaced by the amine, we have a catalysed formation of dinitrogen trioxide, which is still the nitrosating carrier for the amine. These relations are summarised in the annexed scheme.



Mechanisms of aqueous diazotisation . . . . . (20)

In scheme 20, every process except the two marked " fast " has separately been made rate-controlling, and has had its kinetics determined. The figures against the arrows are the numbers of the relevant kinetic equations, as listed in sub-section (1a). All these processes are bimolecular nucleophilic substitutions S_N2.

(2) Recent Reports on the Kinetics of Nitrosation

The first of several summaries of the findings now particularised was published in 1950. Since then, a number of papers have appeared, which our work seems to have influenced, on the kinetics and mechanism of one or another of the forms of nitrosation. Some of these reports confirm our conclusions, whilst others leave discrepancies, which need consideration.

(a) N-*Nitrosation*: *Concordant Reports.*—There have been several by Schmid. He and Woppmann repeated the diazotisation of aniline at low acidities, which they set with added nitric acid.[2] They confirmed equation (2), and the transition between equations (1) and (2); and they obtained, for the rate constant k_2'' of equation (2) at 0°, a value 0·92 sec.$^{-1}$ mole^{-1} l., in good agreement with our comparable value given in Part II. Schmid and Muhr's early work on chloride catalysis has been extended by Schmid and Pfeiffer to include deamination,[3] and by Schmid and Hallaba within the field of diazotisation.[4] These kinetics always followed equation (5). Schmid and his co-workers were evidently unable, just as we were in chloride-catalysis, to realise the transition to equation (6).

(b) N-*Nitrosation*: *Discrepant Reports.*—Okano and Ogato have reported [5] on the diazotisation of aniline in sulphuric acid over the pH range 0·6—3·3. According to our conclusions, the reaction should follow at first the third-order equation (1), and later the second-order equation (2), as acidity is decreased over this range. It is curious that, although Okano and Ogata refer to our paper of 1950, in which the main point was the

[1] Hughes, Ingold, and Ridd, *Nature*, 1950, **166**, 642; Ingold, *Bull. Soc. chim. France*, 1952, **19**, 667; " Structure and Mechanism in Organic Chemistry," Cornell Univ. Press, 1953, p. 398; cf. Ridd, Thesis, London, 1951.

[2] Schmid and Woppmann, *Monatsh.*, 1952, **83**, 346; cf. Schmid, *ibid.*, 1954, **85**, 424.

[3] Schmid and Pfeiffer, *ibid.*, 1953, **84**, 829, 842.

[4] Schmid and Hallaba, *ibid.*, 1956, **87**, 560.

[5] Okano and Ogata, *J. Amer. Chem. Soc.*, 1953, **75**, 5175.

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change from third-order to second-order kinetics within their pH range, they make no reference to the point itself, and continue their paper as if in ignorance of it. Without citing any of their own experimental readings, or offering any new evidence as to the extent to which equation (1) is obeyed in their conditions, they record, for their whole pH range, third-order constants k_3'', calculated with the integrated form of equation (1). Then, in just that part of the range, pH 2·0—3·3, in which the real kinetic order will be well away from three, they find that their calculated constants (which cannot in fact have been constant) decrease with diminishing acidity; and therefrom they draw the conclusion that the true rate-equation is a fourth-order one,

$$\text{Rate} \propto [H^+][Ph{\cdot}NH_2][HNO_2]^2$$

and that the real nitrosating entity is, not N_2O_3, but $HN_2O_3^+$.

Now this is not sensible. It should be clear from our paper, which they cited, that when acidity is reduced, and the fraction of molecular amine is thereby increased, the rate rises at first proportionally, and then less than proportionally to the amine, until, finally, it stops rising; wherefore, when one calculates third-order constants, so dividing absolute rate *inter alia* by the amine concentration, one divides by a quantity which becomes progressively too large, and so one produces answers which become progressively too small, as the acidity is diminished. That is the origin of Okano and Ogata's apparent order of unity in hydrogen ions. We are not saying, of course, that $HN_2O_3^+$ does not exist, or never would nitrosate. But we do say that these authors had no evidence for either its existence or its effectiveness; and that, neither under their conditions, nor under any hitherto investigated conditions, does it function comparably in extent to N_2O_3 in the diazotisation of aniline.

The other discrepancies can mostly be traced to the all too common idea that one buffer is as good as another, so long as both give the same pH. Specific effects of buffer anions should be expected in our reactions, and we have emphasised the need for circumspection in the selection of buffers, and for the careful control of their specific effects (Part III). Difficulties through the neglect of such precautions first arose in a paper by Dusenbury and Powell, who claimed that T. W. J. Taylor's original observation of kinetic equation (1) in deamination was incorrect,[6] a claim which led us to publish a statement that we had repeated Taylor's work and had found it perfectly correct.[7] Dusenbury and Powell, using a phosphate buffer, were replacing the normal deaminating agent, dinitrogen trioxide, by a new one, a nitrosyl phosphate. They gave equation (4) as their kinetic expression, but there can be no doubt that it should have contained a phosphate-concentration factor, corresponding formally to the halide factor in equation (5).

Li and Ritter report [8] that the decomposition of nitrosyldisulphonate ion, $NO(SO_3)_2^-$, follows equation (2). But they were working in concentrated acetate solution, though without regard for its specific effects; and so the more important kinetic equation in their conditions must really have been equation (3). This seems to be the more certain, inasmuch as the rate constant k_2'', calculated for equation (2) from their results, is about 6 times larger than our value of that quantity. The conclusion that dinitrogen trioxide was the reagent remains, though it was formed, not by self-dehydration, but by a catalytic mechanism, and its primary reaction cannot have been a simple *N*-nitrosation. Li and Ritter also report that the deamination of sulphamate ion, $NH_2{\cdot}SO_3^-$, follows equation (4). Here again the work was done in acetate buffers, the specific effects of which were disregarded. It is therefore not known whether the kinetic equation should have contained an acetate-concentration factor, like the halide-concentration factor of equation (5). The open question here is whether the nitrosating agent was the nitrous acidium ion or nitrosyl acetate. It is unlikely that it was, as they assume, the nitrosonium ion.

[6] Dusenbury and Powell, *J. Amer. Chem. Soc.*, 1951, **73**, 2269.
[7] Austin, Hughes, Ingold, and Ridd, *ibid.*, 1952, **74**, 555.
[8] Li and Ritter, *ibid.*, 1953, **75**, 3024.

(c) O-*Nitrosation*: *Concordant Reports.*—Bunton, Llewellyn, and Stedman [9] have noted that isotopically marked oxygen is exchanged between nitrous acid and water in accordance with kinetic equation (2). This means that dinitrogen trioxide is the carrier of the isotopic exchange. The equilibrium in the dehydration of nitrous acid in water being on the side of nitrous acid, the dinitrogen trioxide is formed slowly, and nitrosates water rapidly—just as it nitrosates aniline rapidly, when we supply sufficient molecular aniline. The rate of formation of dinitrogen trioxide, as measured at 0° through the diazotisation of aniline, is 0·85 sec.$^{-1}$ mole^{-1} l. at low ionic strengths, and 0·78 sec.$^{-1}$ mole^{-1} l. at the ionic strength 0·1M, these values (Parts II and III) being somewhat dependent on the figure taken for the acidity constant of nitrous acid. Bunton, Llewellyn, and Stedman used 0·4—1·0M-sodium nitrite, to which they added a somewhat small proportion of perchloric acid, thereby liberating an equivalent quantity of practically undissociated nitrous acid in the excess of nitrite; and for the rate-constant of exchange at 0°, they found 0·53 sec.$^{-1}$ mole^{-1} l., a firm figure not dependent on the acidity constant of nitrous acid. These rates may all be consistent to within the somewhat small uncertainty of the acidity constant. For at low ionic strengths, when the nitrous acid is considerably ionised, its self-dehydration must be subject to a negative salt effect; which will die out, as indeed Bunton, Llewellyn, and Stedman verified for their conditions, when enough of a common ion, whether hydrogen or nitrite, is added to suppress ionisation of nitrous acid; but which will, before that stage is reached, have reduced the rate of self-dehydration to well below its value at low ionic strengths.

Allen [10] has investigated the hydrogen-ion catalysed hydrolysis of several alkyl nitrites by dilute ($\sim 10^{-3}$M) perchloric acid in aqueous dioxan. As nitrosyl–oxygen fission was established, the reaction is a nitrosation of water. Allen's kinetic equation corresponds to our hydrogen-ion-catalytic equation (4), but with alkyl nitrite replacing nitrous acid, and water replacing amine. This shows that the nitrosating agent is either the nitrous esterium ion, NO·OHR$^+$, or the nitrosonium ion, NO$^+$, formed from it. As in our case of hydrogen-ion catalysis, as discussed in sub-sections 1d and 1f, the crux of the problem is to distinguish between these possibilities. Allen proceeded as we have done: he studied halide-ion catalysis, and showed that this could be used to measure the rate of bimolecular substitution of the halide ion in the nitrous esterium ion to give nitrosyl halide; and then, by arguments of comparison, he was able to conclude that, in the absence of halide ion, water reacts with the nitrous esterium ion, and not with the nitrosonium ion. Thus the nitrous esterium ion, like the nitrous acidium ion, does its nitrosating by S_N2, and not by S_N1, substitutions. Certainly, we should expect these two conjugate acids to behave quite similarly, and thus Allen's conclusions and ours, concerning hydrogen-ion catalysis in nitrosation, are mutually confirmatory.

(d) O-*Nitrosation*: *Discrepant Report.*—Anbar and Taube have also examined oxygen exchange between nitrous acid and water.[11] They claim kinetics which are at variance with equation (2), and are even incompatible with the occurrence of the self-dehydration which that equation represents, but are, on the other hand in agreement with equation (4)—with the difference that water replaces amine. They also claim that this result is not an artefact of the phosphate buffer used; and they interpret it as due to nitrosation by the nitrosonium ion, though they did nothing to distinguish this from the nitrous acidium ion, and insufficient to distinguish these from nitrosyl dihydrogen and monohydrogen phosphate. However, they deduce that our conclusions concerning the reactions of nitrous acid with amines are "incomplete if not incorrect," and that their results "indicate the necessity for re-examining the reactions in question." This necessity is, in their opinion, made the more apparent by the "paradoxes" among amine reactions, particularly the "direct contradiction" that in some circumstances they are of first and

[9] Bunton, Llewellyn, and Stedman, *Nature*, 1955, **175**, 83.
[10] Allen, *J.*, 1954, 1968.
[11] Anbar and Taube, *J. Amer. Chem. Soc.*, 1954, **76**, 6243.

in some of second order in nitrous acid. They argue that Dusenbury and Powell's first-order result (like their own) is not due to phosphate catalyses, but that, on the other hand, our second-order reaction (2) is fallacious. Two of their reasons for these conclusions are, first, that Li and Ritter's rate-constant for the decomposition of nitrosyldisulphonate ion would make reaction (2) obvious in Dusenbury and Powell's (and their own) conditions, and, secondly, that Li and Ritter, and Schmid and Woppmann, obtained disagreeing rate-constants for reaction (2).

Now the most obvious point about the actual figures given by Anbar and Taube is that their constants for the equation corresponding to (4) are not even approximately constant. They vary widely with the pH. They vary with the concentration of the buffer, and become changed in the experiments in which the usual phosphate buffer was replaced by an acetate or a phthalate buffer of similar pH. It appears, then, that there is some invalidity in the allowance for the dependence of rate on hydrogen ion in Anbar and Taube's rate-expression, in which, also, a buffer-ion concentration should have appeared. In a forthcoming paper by Bunton, Llewellyn, and Stedman, it will be shown [12] more quantitatively that Anbar and Taube's rates are phosphate-catalysed, and that the observed reductions of kinetic order in nitrous acid below two are due to the production of a nitrosyl phosphate, which, when in sufficient concentration, takes over the nitrosating function. In the same paper it will be shown that even acetate buffers will act similarly if their concentration is high enough. It is also shown that the relative efficiency of dinitrogen trioxide and of a general nitrosyl compound, as nitrosating agents, depends on what is being nitrosated, *e.g.*, water or amine. Furthermore, we have seen that the relative efficiency with which a general nitrosyl compound nitrosates water, amine, and nitrite ion depends on the nature of the nitrosyl compound. In this somewhat involved situation, which the use of buffers creates, the arguments of Anbar and Taube mean nothing: they were doing what Dusenbury and Powell had previously been criticised for doing, *viz.*, treating buffers as chemically immaterial except for the control of pH. That is why it did not strike them that Li and Ritter's rate was a buffer-catalysed rate, whereas Schmid and Woppmann's rate was not; and that the former rate has nothing to do with the *self*-dehydration of nitrous acid. It would be useful to have a buffer, whose anions were basic, yet not otherwise nucleophilic,[13] but the phosphate buffer does not happen to be such.

Anbar and Taube offer a third objection to equation (2) and its interpretation with respect to amine nitrosations. This is based on the results of their examination of oxygen exchange accompanying the diazotisation of aniline, in conditions which they considered would ensure exclusive diazotisation according to equation (2), supposing that this equation had any validity. They noted that, since the re-hydration of the formed dinitrogen trioxide would in that case be completely intercepted by its reaction with aniline, no oxygen exchange between nitrous acid and water should be observed. Actually, they found an especially rapid exchange in the conditions of these experiments.

But the conditions were wrong: in these particular experiments, Anbar and Taube changed their usual phosphate buffer for a phthalate buffer, using such a concentration that most of the diazotisation must have followed equation (3), rather than equation (2). And when we examine the detailed meaning of equation (3), as expressed by scheme (12) in sub-section (1c), we see that it requires oxygen exchange to be much faster than the formation of dinitrogen trioxide, and therefore much faster than the already buffer-accelerated diazotisation. Again, Anbar and Taube were not realising clearly that they were dealing with a buffer-catalysed reaction, having no relation to the self-dehydration of nitrous acid.

We thank Dr. C. A. Bunton and Dr. G. Stedman for very helpful discussions.

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[12] Bunton, Llewellyn, and Stedman, *Chem. Soc. Special Publ.*, No. 10, to be published.
[13] Cf. Pritchard and Long, *J. Amer. Chem. Soc.*, 1957, **79**, 2365.

19. *Niobium and Tantalum Mixed Alkoxides.*

By D. C. Bradley, B. N. Chakravarti, A. K. Chatterjee, W. Wardlaw, and (Miss) A. Whitley.

A number of volatile mixed alkoxides of tantalum of the type $Ta(OR)(OR')_4$, where R is a primary, secondary, or tertiary alkyl group and R′ is secondary or tertiary, have been prepared by alcohol interchange in the presence of excess of R′OH. The corresponding type of compound, with R′ = *tert.*-butyl, for niobium was unstable, giving rise to $Nb_2O(OBu^t)_8$ and $NbO(OBu^t)_3$. The penta*iso*propoxides of niobium and tantalum were also prepared.

In attempting to prepare tantalum penta*iso*propoxide by alcohol interchange of tantalum pentaethoxide with *iso*propyl alcohol we obtained a crystalline mixed alkoxide $Ta(OEt)(OPr^i)_4$ which sublimed unchanged under reduced pressure. The mixed alkoxide still remained despite prolonged treatment with excess of *iso*propyl alcohol. However, tantalum penta*iso*propoxide was obtained directly by the reaction of tantalum pentachloride, *iso*propyl alcohol, and ammonia. Similarly, tantalum penta-*tert.*-butoxide had been obtained [1] from the pentachloride by the ammonia method, yet the action of excess of *tert.*-butyl alcohol on tantalum pentaethoxide gave the volatile crystalline $Ta(OEt)(OBu^t)_4$. Further work revealed that the formation of tantalum mixed alkoxides is a general feature of alcohol interchange when the alcohol in excess is a secondary or tertiary alcohol, *viz.*,

$$Ta(OR)_5 + 4R'OH \longrightarrow Ta(OR)(OR')_4 + 4ROH$$

Some data on these compounds and the penta*iso*propoxide, penta-*tert.*-butoxide and penta-*tert.*-amyloxide are given in Table 1. The molecular complexities shown in parentheses are assumed values. For example, both $Ta(OEt)(OBu^t)_4$ and $Ta(OBu^t)_5$ were found to be monomeric, so $Ta(OPr^i)(OBu^t)_4$ must also be monomeric.

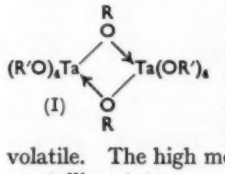
Table 1.

Compound	M. p.	Volatility *	Mol. complexity
$Ta(OMe)(OPr^i)_4$	70°	81°/0·07 mm.†	1·84
$Ta(OEt)(OPr^i)_4$	—	130/0·1 †	1·16
$Ta(OPr^i)_5$	84	122/0·1	0·99
$Ta(OMe)(OBu^t)_4$	110	96/0·05 †	1·00
$Ta(OEt)(OBu^t)_4$	96	84/0·05,† 128/5·5	0·99
$Ta(OPr^i)(OBu^t)_4$	94	86°/0·02 mm.	(1·0)
$Ta(OBu^t)_5$	110	82/0·02,† 149·5/5·5	1·01
$Ta(OEt)(OCMe_2Et)_4$	158	170/0·1	(1·0)
$Ta(OPr^i)(OCMe_2Et)_4$	90	139/0·1	(1·0)
$Ta(OCMe_2Et)_5$	—	142/0·1	1·01

* *I.e.*, boiling point or sublimation point (marked †).

The molecular weights were determined cryoscopically in benzene for all compounds except the penta-*tert.*-amyloxide which was determined ebullioscopically. Ebullioscopy gave anomalously high values for the other compounds owing to their appreciable volatility in boiling benzene.

The series $Ta(OR)(OPr^i)_4$, where R = Me, Et, or Pr^i, is of special interest because only one alkoxide group varies and it is the particular group involved in polymerisation by bridging, *i.e.*, inset (I). The results clearly show that the degree of dimerisation decreases with increase in size of the group OR in the order MeO > EtO > Pr^iO, expected on stereochemical grounds. The remaining compounds in Table 1 are monomeric and it is not surprising that they are relatively volatile. The high melting points suggest that these molecules rotate considerably in the crystalline state.



(I)

[1] Bradley, Wardlaw, and Whitley, *J.*, 1956, 1139.

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It is tempting to suggest that the formation of these mixed alkoxides is caused by steric effects because they are only formed where R′ is a branched alkyl group. The failure to replace the OR group in $Ta(OR)(OR')_4$ would then be due to repulsion of the incoming R′OH molecule by the other branched groups attached to the tantalum. This implies that alcohol interchange involves a bimolecular mechanism in which the incoming alcohol molecule becomes co-ordinated to the tantalum in the transition state. However, this simple explanation is inadequate, because, for example, the molecular weight shows that $Ta(OMe)(OPr^i)_4$ is predominantly dimeric. Now the steric hindrance to forming the dimer $Ta_2(OMe)_2(OPr^i)_8$ (assumed to be a binuclear octahedral complex) is very similar to that involved in the activated complex $Pr^iOH \rightarrow Ta(OMe)(OPr^i)_4$ and hence this transition state should be readily attained and interchange ought then to occur. More remarkable is the fact that interchange occurred between tantalum penta-*tert.*-butoxide and *tert.*-amyl alcohol with the formation of the mixed tertiary alkoxide $Ta(OBu^t)_2(OCMe_2Et)_3$. This being the case it seems probable that the treatment of, say, $Ta(OMe)(OPr^i)_4$ with excess of *iso*propyl alcohol leaves the methoxide group attached to tantalum because the *iso*propoxide groups are preferentially replaced. Amongst more work required to solve this problem is a knowledge of the structure of the monomeric tantalum penta-alkoxides.

Niobium resembled tantalum in behaviour in some of these reactions but differed in others. For example, niobium pentaethoxide with excess of *iso*propyl alcohol gave a niobium ethoxide *iso*propoxide. Also, niobium penta*iso*propoxide was readily prepared from the pentachloride, *iso*propyl alcohol, and ammonia. The penta*iso*propoxide (sublimes at 60—70°/0·1 mm.) is monomeric and apears to be more volatile than the corresponding tantalum compound. However, when niobium pentaethoxide was treated with *tert.*-butyl alcohol the ethoxide was all replaced but the product was an oxide *tert.*-butoxide near $Nb_2O(OBu^t)_8$ which, at 110—130°/0·01 mm., gave a sublimate of mainly $NbO(OBu^t)_3$. In a reaction of niobium *iso*propoxide with *tert.*-butyl alcohol in which the temperature did not exceed 40° the product, a mixture of $Nb(OPr^i)(OBu^t)_4$ and $Nb_2O(OBu^t)_8$, showed that decomposition had occurred. This behaviour of niobium alkoxides with *tert.*-butyl alcohol is similar to that of niobium pentachloride with *tert.*-butyl alcohol in the presence of pyridine and ammonia.[2] No penta-*tert.*-butoxide was isolated, but a niobium oxide *tert.*-butoxide was obtained. The present results show that niobium *tert.*-butoxides are unstable irrespective of whether they are prepared from the pentachloride or by alcohol interchange on a penta-alkoxide.

Experimental

Preparation of Mixed Alkoxides of Tantalum.—Tantalum penta-methoxide, -ethoxide, -*tert.*-butoxide, and -*tert.*-amyloxide were prepared as already described.[1,3] The mixed alkoxides were then obtained by alcohol interchange in benzene with removal of the liberated

Table 2.

R	$Ta(OR)_5$ (g.)	R′	R′OH (g.)	C_6H_6 (c.c.)	$Ta(OR)(OR')_4$ (g.)	OR (%) Found	OR (%) Calc.	Ta (%) Found	Ta (%) Calc.
Me	3·5	Pr^i	35·0	150	4·5	—	—	40·4	40·4
Et	4·0	Pr^i	37·8	150	4·5	—	—	39·2	39·1
Me	3·5	Bu^t	150 *	—	5·0	6·0	6·1	35·7	35·9
Et	3·7	Bu^t	150 *	—	5·1	8·7	8·7	35·0	34·9
Pr^i	3·0	Bu^t	180 *	—	3·4	11·7	11·1	33·8	34·0
Et	3·0	CMe_2Et	53·6	100	4·0	7·9	7·8	31·4	31·5
Pr^i	4·0	CMe_2Et	10·5	50	4·5	9·8	10·0	30·7	30·7

* Benzene–*tert.*-butyl alcohol azeotrope.

alcohol by azeotropic fractional distillation. The solution was evaporated to dryness under reduced pressure and the solid product sublimed in a molecular still. Details are given in Table 2.

[2] Bradley, Chakravarti, and Wardlaw, *J.*, 1956, 4439.
[3] Bradley, Wardlaw, and Whitley, *J.*, 1955, 726.

Preparation of Tantalum Pentaisopropoxide.—Tantalum pentachloride (5·0 g.) was added to *iso*propyl alcohol (15 c.c.) and benzene (100 c.c.) and the solution was treated with excess of ammonia. After filtering off the ammonium chloride and evaporating the filtrate to dryness under reduced pressure we obtained white crystals (5·2 g.) of the *pentaisopropoxide*, m. p. 84°; it was distilled at 122°/0·1 mm. [Found: Ta, 37·8; Pr^iO, 61·8. $Ta(OPr^i)_5$ requires Ta, 38·0; Pr^iO, 62·0%].

Reaction of Tantalum tert.-*Butoxide with* tert.-*Amyl Alcohol.*—To the solution of tantalum *tert.*-butoxide (3 g.) in benzene (50 c.c.) was added *tert.*-amyl alcohol (5·0 c.c.) and the mixture was fractionally distilled. The appearance of the benzene–*tert.*-butyl alcohol azeotrope indicated a replacement. When no more azeotrope was produced the solution was evaporated under reduced pressure to give *tantalum tri*-tert.-*amyloxide di*-tert.-*butoxide* as a viscous liquid (3·2 g.) [Found: Ta, 30·7. $Ta(OBu^t)_2(OCMe_2Et)_3$ requires Ta, 30·8%].

Preparation of Niobium Pentaisopropoxide.—Niobium pentachloride (28·7 g.) was added to *iso*propyl alcohol (100 c.c.) and benzene (250 c.c.) and the solution was treated with excess of ammonia. After the removal of ammonium chloride and solvent in the usual manner a grey-blue solid (30·6 g.) remained. This was washed four times with cold *iso*propyl alcohol (25 c.c.) to remove the colour and the residue was sublimed at 60—80°/0·1 mm. The white sublimate of *niobium pentaisopropoxide* recrystallised from boiling *iso*propyl alcohol [Found: Nb, 24·1; Pr^iO, 75·0. $Nb(OPr^i)_5$ requires Nb, 24·0; Pr^iO, 76·0%].

Reaction of Niobium Ethoxide with tert.-*Butyl Alcohol.*—Niobium pentaethoxide [4] (3·9 g.) in benzene (150 c.c.) was treated with *tert.*-butyl alcohol until no more benzene–ethyl alcohol azeotrope could be separated by fractional distillation. Removal of excess of *tert.*-butyl alcohol and solvent under reduced pressure left crystals of the *oxide* tert.-*butoxide* (3·8 g.) [Found: Nb, 24·1; EtO, 0. $Nb_2O(OBu^t)_8$ requires Nb, 23·6%]. This product was sublimed at 110—130°/0·01 mm. in a molecular still to yield another *oxide* tert.-*butoxide* [Found: Nb, 27·8. $NbO(OBu^t)_3$ requires Nb, 28·3%]. A small amount of non-volatile residue with a high niobium content (39·7%) remained.

Reaction of Niobium iso*Propoxide with* tert.-*Butyl Alcohol.*—Niobium penta*iso*propoxide (2·5 g.) was dissolved in benzene–*tert.*-butyl alcohol azeotrope (100 c.c.) at room temperature and the solvent and mixture of alcohols were then evaporated under reduced pressure below 45°. White crystals of the *oxide* tert.-*butoxide* iso*propoxide* (3·3 g.) remained [Found: Nb, 21·3; Pr^iO, 4·8. $Nb_3O(OPr^i)(OBu^t)_{12}$ requires Nb, 22·6; Pr^iO, 4·8%].

Molecular Weight.—An all-glass freezing-point apparatus incorporating a Beckmann thermometer was used with benzene as solvent. Results are given in Table 3.

TABLE 3.

Compound	Wt. of cpd. (g.)	Wt. of C_6H_6 (g.)	F. p. depression	*M* Found	*M* Calc.
$Ta(OMe)(OPr^i)_4$	0·5654	39·12	0·089°	829·5	448·3
	0·8082	,,	0·129	818·0	,,
$Ta(OEt)(OPr^i)_4$	0·3874	45·63	0·081	536·0	462·3
	0·7991	,,	0·166	539·0	,,
$Ta(OPr^i)_5$	0·250	12·35	0·220	472	476
	0·426	,,	0·370	472	,,
	0·622	,,	0·540	473	,,
$Ta(OMe)(OBu^t)_4$	1·007	43·87	0·239	492·0	504·4
	1·878	,,	0·440	498·0	,,
$Ta(OEt)(OBu^t)_4$	0·4255	57·33	0·075	507·0	518·4
	0·9628	,,	0·165	521·0	,,
$Nb(OPr^i)_5$	0·9349	40·60	0·305	386·5	388·4
	1·8236	,,	0·584	393·8	,,

We thank the Universities of Bihar and Patna for study leave (to B. N. C. and A. K. C.).

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[4] Bradley, Chakravarti, and Wardlaw, *J.*, 1956, 2381.

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20. *Experiments relating to Phthiocerol. Part II.* Synthesis of (+)-6-Methoxy-6-methylnonanoic Acid.*

By J. W. Lewis and N. Polgar.

(+)-6-Methoxy-6-methylnonanoic acid has been synthesised, with (+)-2-methoxy-2-methylpentanoic and (+)-6-methoxy-6-methyl-5-oxononanoic acid as intermediates. The synthetic acid is not the enantiomer of the lævorotatory C_{11} methoxy-acid arising on oxidation of phthiocerol.

Earlier work [1] showed that phthiocerol, on oxidation with chromic acid, affords *n*-tetracosanoic acid together with a C_{11} methoxy-acid. The isolation of these oxidation products, together with other evidence which included the formation of a β-diketone by mild oxidation of phthiocerol, indicated that the latter is a tetratriacontane-9 : 11-diol containing a methyl and a methoxyl group, probably both attached at $C_{(4)}$ (cf. I). This suggested that the C_{11} oxidation product (found to be lævorotatory [2]) might be 6-methoxy-6-methylnonanoic acid (II), and it was of interest to prepare an optically active specimen of this acid for comparison. The present communication records the synthesis of its (+)-form.

(I) $CH_3 \cdot [CH_2]_{22} \cdot CH(OH) \cdot CH_2 \cdot CH(OH) \cdot [CH_2]_4 \cdot CMe(OMe) \cdot [CH_2]_2 \cdot CH_3$

(II) $CH_3 \cdot [CH_2]_3 \cdot CMe(OMe) \cdot [CH_2]_4 \cdot CO_2H$

The starting material was pentan-2-one which was converted, *via* its cyanohydrin (III), into methyl 2-hydroxy-2-methylpentanoate (IV); the latter was treated with methyl iodide–silver oxide. Only partial methylation occurred and after three repetitions of this procedure the product still contained unchanged hydroxy-ester. Pure 2-methoxy-2-methylpentanoic acid (V) was obtained from this mixture by hydrolysis, and treatment of the liberated acids with lead tetra-acetate: this left the α-methoxy-acid unchanged, but converted the α-hydroxy-acid into pentan-2-one. In further experiments it was found that the methoxy-acid can be readily separated from the hydroxy-acid by crystallisation of the quinine salts from acetone. Moreover, the quinine salt derived from the methoxy-acid also proved satisfactory for the resolution of the latter, affording the (+)-enantiomer, $[\alpha]_D$ +24·3°.

(III) $CH_3 \cdot [CH_2]_3 \cdot CMe(OH) \cdot CN$ $\quad$ $CH_3 \cdot [CH_2]_3 \cdot CMe(OH) \cdot CO_2Me$ (IV)

(V) $CH_3 \cdot [CH_2]_3 \cdot CMe(OMe) \cdot CO_2H$ $\quad$ $CH_3 \cdot [CH_2]_3 \cdot CMe(OMe) \cdot CH_2 \cdot OH$ (VI)

We then turned to the conversion of the (+)-enantiomer of 2-methoxy-2-methylpentanoic acid (V) into the higher homologue (II). The malonic ester method was examined first. In a model experiment the acid (V) was converted, by reduction with lithium aluminium hydride, into 2-methoxy-2-methylpentan-1-ol (VI), and this into its toluene-*p*-sulphonate. Condensation with ethyl sodiomalonate, followed by hydrolysis of the resulting substituted malonic ester, then gave only small amounts of acidic material; moreover, on attempted decarboxylation of the latter the product contained according to its infrared spectrum a γ-lactone and no methoxyl group.

Then (+)-2-methoxy-2-methylpentanoic acid (V) was converted into the acid chloride which, with ethyl sodio-acetoacetate, followed by sodium methoxide (cf. Ställberg-Stenhagen and Stenhagen [3]), afforded (+)-(methyl 4-methoxy-4-methyl-3-oxoheptanoate) (VII). The sodio-derivative of this ester, on reaction with ethyl β-iodopropionate under the conditions described by Ställberg-Stenhagen and Stenhagen,[3] followed by hydrolysis

* Part I, *J.*, 1955, 3971.

[1] Hall, Lewis, and Polgar, *J.*, 1955, 3971.
[2] Drayson, Lewis, and Polgar, unpublished work.
[3] Ställberg-Stenhagen and Stenhagen, *Arkiv Kemi, Min., Geol.*, 1944, **19**, *A*, No. 1; and later papers.

and ketonic cleavage, gave (+)-6-methoxy-6-methyl-5-oxononanoic acid (VIII), $[\alpha]_D$ +20·2°.

It remained to convert the keto-acid (VIII) into the deoxy-acid (II). An attempt to reduce the keto-acid by the Wolff–Kishner (Huang-Minlon) procedure cleaved the methoxyl group with the formation of unsaturated material (cf. the formation of olefins noted [4] on Wolff–Kishner reduction of α-ketols). Removal of the keto-group by preparation of a thioketal, followed by treatment with Raney nickel,[5] also failed owing to loss of the methoxyl group during the formation of the thioketal. Finally the enol lactone (IX), obtained from the (+)-form of the acid (VIII) by the action of acetic anhydride and sodium acetate,[7] passed on hydrogenation [6] into the acid (II), $[\alpha]_D$ +2·8°.

(VII) $CH_3\cdot[CH_2]_2\cdot CMe(OMe)\cdot CO\cdot CH_2\cdot CO_2Me$

(VIII) $CH_3\cdot[CH_2]_2\cdot CMe(OMe)\cdot CO\cdot[CH_2]_3\cdot CO_2H$

(IX) $CH_3\cdot[CH_2]_2\cdot CMe(OMe)\cdot C{=}CH\cdot[CH_2]_2\cdot CO$ (O)

This acid and the C_{11} oxidation product of phthiocerol showed differences in their infrared absorption spectra, and in m. p. and *X*-ray powder photographs (kindly taken by Mrs. D. M. Hodgkin, F.R.S.) of their *S*-benzylthiuronium salts. A notable feature in the infrared spectra was a difference in the position of the bands attributable to the methoxyl group: the synthetic acid, possessing a tertiary methoxyl group, absorbed at 1075 cm.$^{-1}$, whereas the oxidation product showed a band at 1093 cm.$^{-1}$. It is noteworthy that this band corresponded to the position found in another investigation [8] for branched-chain aliphatic compounds with a secondary methoxyl group. Experiments designed to obtain further evidence by degradation of the C_{11} oxidation product will be described later.

Experimental

Optical rotations were determined for homogeneous liquids in a 0·5-dm. tube, and infrared spectra for natural films, unless otherwise stated.

Pentan-2-one Cyanohydrin (III).—Pentan-2-one (400 g.) was added to a solution of sodium pyrosulphite (750 g.) in water (400 c.c.), and the precipitated bisulphite compound collected. To an ice-cooled, stirred suspension of the latter in a little water a solution of potassium cyanide (700 g.) in water (800 c.c.) was gradually added, and stirring continued for 1 hr.; the upper layer was then separated. The aqueous mixture was extracted with ether, and the dried ($MgSO_4$) extract evaporated (before all the ether had been removed, 10 c.c. of sulphuric acid were added). Distillation of the combined liquids through a Vigreux column (20 c.c.) afforded, after a forerun (90 g.; mainly pentan-2-one), *n*-pentan-2-one cyanohydrin (410 g.; 78%), b. p. 102°/19 mm., n_D^{18} 1·4207. Ultée [9] gives b. p. 100°/21 mm. and n_D^{13} 1·42585.

Methyl 2-Hydroxy-2-methylpentanoate (IV).—A mixture of the above cyanohydrin (170 g., 1·5 mol.), dry methanol (56 g., 1·75 mol.), light petroleum (b. p. 40—60°; 100 c.c.), and dry ether (100 c.c.) was saturated with dry hydrogen chloride at 0°. The resulting homogeneous mixture was left overnight in a refrigerator; the imidoate hydrochloride crystallised. The crystals were collected, washed with light petroleum, and, without further purification, decomposed with water (300 c.c.). The crude product, isolated by ether-extraction, was distilled through a Vigreux column (30 c.c.) to give methyl 2-hydroxy-2-methylpentanoate (91 g.), b. p. 70—70·5°/19 mm., n_D^{20} 1·4193, and a higher-boiling fraction, b. p. 72—103°/19 mm. (45 g.; largely unchanged cyanohydrin); the latter, on repetition of the above methanolysis procedure, gave further amounts of the hydroxy-ester. Heilmann [10] gives b. p. 65—66°/15 mm. for methyl 2-hydroxy-2-methylpentanoate obtained by a different procedure.

[4] Barton and Robinson, *J.*, 1954, 3045; and the literature quoted there.
[5] Wolfrom and Karabinos, *J. Amer. Chem. Soc.*, 1944, **66**, 909; Hauptmann, *ibid.*, 1947, **69**, 562.
[6] Cf. Jacobs and Scott, *J. Biol. Chem.*, 1930, **87**, 601; 1931, **93**, 139.
[7] Cf. Woodward, Sondheimer, Taub, Heusler, and McLamore, *J. Amer. Chem. Soc.*, 1952, **74**, 4223.
[8] Morgan and Polgar, unpublished work.
[9] Ultée, *Rec. Trav. chim.*, 1909, **28**, 1.
[10] Heilmann, *Bull. Soc. chim. France*, 1929, **45**, 412.

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2-Methoxy-2-methylpentanoic Acid (V).—The preceding hydroxy-ester (32·5 g.) was refluxed with methyl iodide (50 c.c.) and silver oxide (78 g.; added in five portions during 7 hr.). The mixture was filtered while hot, and the silver salts, after being washed with ether, were extracted with hot chloroform. Removal of the solvents gave a product which showed a weak band at 1087 cm.$^{-1}$ (OMe) and strong hydroxyl absorption. After three further methylations by the above procedure the product was hydrolysed by refluxing it with aqueous-methanolic (1 : 5) potassium hydroxide (8%); the bulk of the methanol was then removed, and the liberated acid isolated by ether-extraction. A 13-g. portion of this product was dissolved in dry benzene (200 c.c.) and oxidised by lead tetra-acetate (11 g.; added in two portions) at 60° (bath) for 3 hr. The mixture was then acidified with hydrochloric acid, and the product isolated by separation of the benzene layer and extraction of the aqueous phase with ether. Distillation of the combined organic layers gave *2-methoxy-2-methylpentanoic acid* (6 g.), b. p. 117°/25 mm. (Found: C, 57·6; H, 10·0. $C_7H_{14}O_3$ requires C, 57·5; H, 9·7%).

Resolution of 2-Methoxy-2-methylpentanoic Acid.—In a preliminary experiment a 0·95-g. sample of the crude acid, resulting from two methylations of methyl 2-hydroxy-2-methylpentanoate and subsequent hydrolysis as described in the preceding section, was dissolved in hot acetone (10 c.c.), and quinine (2·2 g.) was gradually added; the resulting solution was filtered and left overnight. The quinine salt which separated as fine needles was recrystallised from acetone, then decomposed with dilute hydrochloric acid: the liberated acid was isolated by ether-extraction and distillation. Its infrared spectrum showed a strong methoxyl band, and no absorption due to the presence of hydroxyl.

The above procedure was used to prepare the quinine salt from a larger batch of the acid (160 g.). After seven recrystallisations of the quinine salt (261 g.) from acetone, the regained acid (12·2 g.) had α_D^{14} +12·09°. This was again converted into the quinine salt which after one recrystallisation from acetone gave acid (7·5 g.) having α_D^{14} +12·26°, $[\alpha]_D^{14}$ +24·04°. The mother-liquors of the last recrystallisation of the quinine salt yielded 3·8 g. of acid having α_D^{14} +11·3°. This was converted into the quinine salt which after two recrystallisations gave acid (0·92 g.) with $\alpha_D^{9·5}$ +12·80°, $\alpha_D^{11·5}$ +12·64°. A further formation and recrystallisation of the quinine salt gave on decomposition the (+)-acid (0·42 g.), $\alpha_D^{11·5}$ +12·65°, α_D^{15} +12·39°, $[\alpha]_D^{15}$ +24·30°.

2-Methoxy-2-methylpentan-1-ol (VI).—2-Methoxy-2-methylpentanoic acid (5·3 g.) in ether (50 c.c.) was added slowly to a solution of lithium aluminium hydride (3·2 g.) in ether (150 c.c.). The mixture was kept at the room temperature for 1·5 hr., then refluxed for 1 hr. The excess of lithium aluminium hydride was decomposed by ethyl acetate (10 c.c.), and water (10 c.c.) and dilute hydrochloric acid (50 c.c.) were added. The ether layer was separated, and the aqueous layer was extracted with ether. The combined ethereal solutions were washed with 5% aqueous potassium hydroxide, and then with water, dried ($MgSO_4$), and distilled, to give *2-methoxy-2-methylpentan-1-ol* (4 g.), b. p. 95—98°/45 mm. (Found: C, 63·6; H, 12·4. $C_7H_{16}O_2$ requires C, 63·6; H, 12·1%).

Attempted Malonic Ester Condensation.—Dry pyridine (4·8 g.) was added with stirring under exclusion of moisture to an ice-cold mixture of 2-methoxy-2-methylpentan-1-ol (3·8 g.) and toluene-*p*-sulphonyl chloride (6·1 g.) during 0·5 hr., and stirring continued for a further hour. After acidification with dilute hydrochloric acid, the mixture was extracted with ether, and the product resulting on evaporation of the extract dried azeotropically (benzene), giving crude 2-methoxy-2-methylpentyl toluene-*p*-sulphonate (7·9 g.) (Found: S, 11·2. $C_{14}H_{22}O_4S$ requires S, 11·2%). This ester (6 g.) was refluxed with ethyl sodiomalonate (from 0·52 g. of sodium, 4·4 g. of ethyl malonate, and 40 c.c. of ethanol) and sodium iodide (5 g.) for 20 hr. After acidification with dilute hydrochloric acid, the product was isolated with the aid of ether, then refluxed with 25% aqueous-methanolic (1 : 1) potassium hydroxide for 4 hr. The solution was acidified and extracted with ether, and the acid fraction (1·3 g.) removed from the ethereal solution with 10% aqueous potassium hydroxide. Decarboxylation of the liberated acid at 150—170° (bath), followed by distillation, yielded a product which showed in its infrared spectrum a band at 1761 cm.$^{-1}$ (γ-lactone), but no bands due to a carboxyl or methoxyl group.

Methyl 4-Methoxy-4-methyl-3-oxoheptanoate (VII).—Thionyl chloride (10·75 g.) in benzene (40 c.c.) was added to an ice-cold mixture of 2-methoxy-2-methylpentanoic acid (10·15 g.) with pyridine (8·8 g.) and benzene (20 c.c.), and the solution was set aside for 1 hr. The solvent and excess of thionyl chloride were removed under reduced pressure at 50° (bath); more benzene was added and, after decantation of the benzene solution from the residue, the process was repeated. The resulting acid chloride in benzene (20 c.c.) was then refluxed for 1 hr. with

ethyl sodioacetoacetate (obtained by refluxing 10·4 g. of ethyl acetoacetate, 1·7 g. of granulated sodium, and 120 c.c. of benzene for 3 hr.). The product was poured into ice-cold dilute sulphuric acid, and the benzene layer separated; the aqueous phase was extracted with ether, and the combined organic extracts were washed with water, dried ($MgSO_4$), and evaporated. The residue (13·5 g.) was kept with sodium (2·1 g.) in dry methanol (75 c.c.) at the room temperature for 6 hr. Acidification and ether-extraction, followed by distillation, gave *methyl 4-methoxy-4-methyl-3-oxoheptanoate* (7·2 g.), b. p. 123—125°/24 mm., n_D^{17} 1·4363 (Found: C, 59·6; H, 8·7. $C_{10}H_{18}O_4$ requires C, 59·4; H, 8·9%).

(+)-2-Methoxy-2-methylpentanoic acid (7·5 g.; α_D^{14} +12·26°) gave by the above procedure the (+)-keto-ester (5·38 g.), α_D^{20} +16·57°.

6-Methoxy-6-methyl-5-oxononanoic Acid (VIII).—Methyl 4-methoxy-4-methyl-3-oxoheptanoate (7·07 g.) was refluxed with ethyl β-iodopropionate (7·95 g.), anhydrous potassium carbonate (10 g.), and dry pentan-2-one (70 c.c.) for 18 hr. After addition of water, the mixture was extracted with ether, and the extract washed with water, and dried ($MgSO_4$); the solvents were then removed under reduced pressure. The residue was kept at room temperature with a solution of potassium hydroxide (10 g.) in water (20 c.c.) and methanol (200 c.c.) for 18 hr. Removal of the bulk of the methanol, followed by acidification, ether-extraction, and distillation gave *6-methoxy-6-methyl-5-oxononanoic acid* (3·12 g.), b. p. 185—190°/23 mm., n_D^{20} 1·4525 (Found: C, 61·0; H, 9·5; OMe, 14·35. $C_{11}H_{20}O_4$ requires C, 61·1; H, 9·2; OMe, 14·35%).

The (+)-form of methyl 4-methoxy-4-methyl-3-oxoheptanoate gave by the same procedure (+)-6-methoxy-6-methyl-5-oxononanoic acid, b. p. 138—139°/0·9 mm., $[\alpha]_D^{19.5}$ +20·2° (*c* 10·07 in Et_2O).

Attempted Reduction of the Keto-acid.—(i) The keto-acid (1·3 g.), when heated with potassium hydroxide (1 g., 85%) hydrazine hydrate (4 g.), and triethylene glycol (20 c.c.) according to the Huang-Minlon procedure,[11] gave on acidification and distillation of the product unsaturated material (Found: C, 69·9; H, 10·5. Calc. for $C_{10}H_{18}O_2$: C, 70·6; H, 10·6%).

(ii) The keto-acid (0·5 g.) was kept with ethanethiol (0·9 g.), freshly fused zinc chloride (0·5 g.), anhydrous magnesium sulphate (2 g.), and benzene (10 c.c.) at the room temperature for 3 hr.; the mixture was then poured into water, and the product isolated by ether-extraction. It showed no methoxyl band in the infrared spectrum.

3 : 4-Dihydro-6-(1-methoxy-1-methylbutyl)-2-pyrone (IX).—A partially active sample of 6-methoxy-6-methyl-5-oxononanoic acid (2 g.; $\alpha_D^{19.5}$ +6·55°, obtained by the procedure described from incompletely resolved starting material) was refluxed with acetic anhydride (30 c.c.) and anhydrous sodium acetate (3 g.) for 18 hr., then poured into water, and extracted with ether; the extract was washed with aqueous sodium carbonate, then with water, dried ($MgSO_4$), and evaporated. Distillation of the residue gave the partially active *enol-lactone* (1·4 g.), b. p. 145—147°/14 mm., $n_D^{19.5}$ 1·4691, α_D^{16} +5·35° (Found: C, 66·2; H, 9·0. $C_{11}H_{18}O_3$ requires C, 66·7; H, 9·1%).

(+)-6-Methoxy-6-methyl-5-oxononanoic acid gave by the same procedure the (+)-enol-lactone with $[\alpha]_D^{19}$ +19·5° (*c* 9·25 in Et_2O).

6-Methoxy-6-methylnonanoic Acid (II).—The above (+)-enol-lactone gave, on hydrogenation in ethanol at atmospheric pressure and room temperature in the presence of platinic oxide, (+)-*6-methoxy-6-methylnonanoic acid*, b. p. 190—200° (bath)/15 mm., $n_D^{22.5}$ 1·4428, $[\alpha]_D^{20.5}$ +2·8° (*c* 6·38 in Et_2O) (Found: C, 65·1; H, 11·0. $C_{11}H_{22}O_3$ requires C, 65·3; H, 10·9%). Its *S-benzylthiuronium salt* crystallised from ethanol–water (1 : 2) as colourless needles, m. p. 135° (Found: C, 62·3; H, 8·6; N, 7·4. $C_{19}H_{32}O_3N_2S$ requires C, 62·0; H, 8·7; N, 7·6%). On admixture with the *S*-benzylthiuronium salt (m. p. 137—139°) of the C_{11} oxidation product of phthiocerol, the m. p. was 131—133°.

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Dyson Perrins Laboratory, Oxford University. [*Received, August 27th*, 1957.]

[11] Huang-Minlon, *J. Amer. Chem. Soc.*, 1946, **68**, 2487.

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21. *Complexes of Octavalent Ruthenium and Osmium with Phosphorus Trifluoride.*

By M. L. Hair and P. L. Robinson.

The complexes $(MO_4)_2,PF_3$ and MO_4,PF_3 are formed by the tetroxides of ruthenium and osmium. Their preparations and properties are described and their relation with the few other compounds of the platinum metals with phosphorus halides is discussed.

Few complexes of phosphorus trifluoride are known, and they are restricted to Group VIII elements. They are the volatile $(PF_3)_2,PtCl_2$ and $(PF_3,PtCl_2)_2$ prepared by Chatt and Williams,[1] Moissan's PtF_2,PF_3,[2] and Wilkinson's $Ni(PF_3)_4$.[3] Of these only the first two were prepared by direct combination with phosphorus trifluoride. Moissan made PtF_2,PF_3 by passing phosphorus pentafluoride over platinum sponge at a dull red heat, and Wilkinson obtained the $Ni(PF_3)_4$ complex by treating the chlorine analogue either with antimony trifluoride or with phosphorus trifluoride under pressure. Chatt and Williams had no evidence of the formation of similar compounds by palladous chloride; indeed the only other phosphorus trihalide complexes reported are $IrCl_3,3PCl_3$,[4] $IrBr_3,3PBr_3$,[4] $PtCl_2,PCl_3$,[5] and $PtCl_2,2PCl_3$.[5]

Exploring the complexes of phosphorus trifluoride with Group VIII elements, we find that whereas neither metallic ruthenium and osmium nor their dioxides react with either phosphorus trifluoride or trichloride, both the trihalides combined with their tetroxides. Ruthenium tetroxide takes up phosphorus trifluoride at about −100° to give $(RuO_4)_2,PF_3$ and then, at 20°, combines with another molecule of the trifluoride to produce RuO_4,PF_3. Osmium tetroxide does the same, except that $(OsO_4)_2,PF_3$ must be heated to 70° before the further addition takes place. It is not possible to cause more phosphorus trifluoride to combine with the 1 : 1 complexes, nor could the reaction leading to their formation from the 2 : 1 complexes be reversed. All the compounds are black and extremely hygroscopic; they decompose without melting when heated at the ordinary pressure and, when kept under reduced pressure, give the metallic oxide and the trifluoride. These properties, and failure to find a liquid in which they dissolve without decomposition, prevented the determination of molecular weight.

By contrast, both phosphorus trichloride and tribromide reduce ruthenium tetroxide with vigour, sometimes explosively; but when the reactions are moderated by controlling the temperature, the black solids produced have compositions indicative of RuO_2,PCl_3 and RuO_2,PBr_3. Osmium tetroxide gives OsO_2,PCl_3. None of these MO_2 compounds can be made by direct addition to the dioxide.

Chatt and Williams advanced cogent reasons for believing that the bonding in their remarkably stable complexes is due to the acceptance of electrons from the filled *d* orbitals of the platinum into the empty *d* orbitals of the phosphorus. It is less certain that this back co-ordination happens with palladium, for palladous chloride cannot be attached to the trifluoride. Neither of the complexes described here has a stability approaching that of the platinum compounds, and it is reasonable to assume that another type of bonding operates. General expectation would be that phosphorus trifluoride should form complexes by direct donation of its lone pair. Both these tetroxides may be assumed to have a vacant *d* orbital and we suggest that this receives the lone pair from the phosphorus. Of the phosphorus tercovalent compounds, phosphorus trifluoride has the largest X–P–X angle, 104° (cf. PCl_3 101°, PBr_3 100°, PI_3 98°, PH_3 93°), which indicates that the lone-pair

[1] Chatt and Williams, *J.*, 1951, 3061.
[2] Moissan, *Bull. Soc. chim. France*, 1891, 484.
[3] Wilkinson, *J. Amer. Chem. Soc.*, 1951, **73**, 5502.
[4] Strecker and Schurigen, *Ber.*, 1909, **42**, 1767.
[5] Schulzenberger, *Bull. Soc. chim. France*, 1872, **17**, 482.

orbital is narrower and reaches further out from the phosphorus atom in the trifluoride than in the other halides. This may contribute to the stability of these phosphorus trifluoride complexes; other factors must play a part, otherwise boron trifluoride would be expected to combine with phosphorus trifluoride. In the absence of structural data it is unprofitable to speculate on the arrangement of the units within the solids which have not been obtained sufficiently crystalline to give an *X*-ray pattern.

Experimental

Materials.—Ruthenium tetroxide was prepared by Martin's method:[6] ruthenium sponge was fused with potassium hydroxide and nitrate to give potassium ruthenate, which was dissolved in the minimum amount of water and treated with a mixture of equal parts of concentrated sulphuric acid and periodic acid from which the ruthenium tetroxide was distilled by heating on a water-bath. The oxide vapour thus obtained was dried by passage through " anhydrone " in a U-tube at 70°, followed by freezing on, and evaporation from, two separate lots of the same desiccant. This was done in a vacuum system from which the pure ruthenium tetroxide was distilled directly into the reaction apparatus, care being taken to prevent the vapour from coming into contact with tap grease or mercury, with both of which it readily reacts.

Osmium tetroxide was made by igniting the metal in a rapid stream of well dried oxygen. It also was transferred to the reaction apparatus in a vacuum, contact with tap grease being avoided.

Phosphorus trifluoride, prepared by the action of phosphorus trichloride on zinc fluoride,[1] was dried by slow passage through concentrated sulphuric acid followed by two traps at −70°.

Apparatus and Preparations.—The reactions were observed in a small vessel holding the solid tetroxide which formed part of a system of known volume, whose temperature could be controlled by a bath. Before the introduction of the reactants it was carefully dried by repeated changes of dry air and flaming out under a vacuum. The uptake of phosphorus trifluoride or other vapour was measured by means of a manometer.

Ruthenium compounds. A smooth reaction began at −100° and a black solid was formed. The pressure decrease indicated a ratio $Ru : PF_3$ of 0·245 g. : 0·107 g., corresponding to $(RuO_4)_2,PF_3$. No further absorption of phosphorus trifluoride took place below 0°, but when the black material was warmed to about 20° the pressure again decreased without, however, observable change in the solid, indicating a ratio $Ru : PF_3$ of 0·245 g. : 0·213 g. for the *compound*, corresponding to RuO_4,PF_3 (Found: Ru, 40·80; F, 20·58. RuO_4,PF_3 requires Ru, 40·25; F, 22·56%). There was no trace of oxygen or phosphorus oxyfluoride after reaction was complete. The former, not being condensed by liquid oxygen, would have given a pressure observable on the manometer, and the latter would have condensed when the reaction bulb was subsequently cooled to −70°.

The 1 : 1 compound had an appreciable vapour pressure of phosphorus trifluoride at 20° and lost this gas when heated under a vacuum, reverting to ruthenium tetroxide. The change from the first to the second compound is irreversible. The second compound is extremely hygroscopic, being rapidly converted into a red liquid by atmospheric moisture. Hydrolysis then supervenes and black, hydrated ruthenium dioxide is precipitated. The typical odour of ruthenium tetroxide is evident, indicating the high valency of the compound.

Osmium compounds. Again a smooth reaction began at −100° with the formation of a black solid. Pressure decrease indicated a ratio $Os : PF_3$ of 0·292 g. : 0·068 g. corresponding to $(OsO_4)_2,PF_3$. There was no further uptake of gas below 60°, at which temperature more phosphorus trifluoride was absorbed until the ratio $Os : PF_3$ of 0·292 g. : 0·13 g. was reached corresponding to OsO_4,PF_3. There was no observable change in the appearance of the solid *compound* (Found: Os, 53·5; F, 16·7. OsO_4,PF_3 requires Os, 55·6; F, 16·66%).

Attempts to make other complexes. Phosphorus trichloride condensed on ruthenium tetroxide and allowed to warm also gave a black solid which, as the temperature rose, was liable to change rapidly in colour and explode, possibly through the formation of an oxide of chlorine. When, however, the temperature was controlled or the reaction was carried out in carbon tetrachloride solution the solid was isolable. Both phosphorus and chlorine were present, and, though it varied a little, the average composition corresponded to RuO_3,PCl_3. Evidently phosphorus trichloride under suitable conditions reduces the tetroxide to the dioxide and forms

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complexes with the latter. Nevertheless it has not been possible to make such a compound directly from the dioxide. Osmium tetroxide, though not so strong an oxidising agent, was also reduced and appears to form the corresponding OsO_2,PCl_2 complex.

Phosphorus tribromide also reacted vigorously and exothermally with ruthenium tetroxide in carbon tetrachloride. The yellow phosphorus oxybromide produced was removed under a vacuum leaving a black residue containing ruthenium, phosphorus, and bromine and was probably a mixture of RuO_2 and RuO_2,PBr_3.

Rather surprisingly, phosphine did not react with osmium tetroxide below 70°, at which temperature there was a slight reduction but no evidence of the addition of phosphine. The effect on ruthenium tetroxide was not examined in view of its greater oxidising properties and a danger of explosion.

As expected of boron trifluoride, this acceptor molecule did not form a complex with RuO_4, OsO_4, or OsF_8 at any temperature between its b. p. (−101°) and 600°.

Analysis.—Fluorine. The analysis of these compounds for phosphorus and fluorine is difficult because they tend to lose phosphorus trifluoride on attack by fused or aqueous sodium carbonate or perchloric or nitric acids. The only satisfactory way of opening the complexes was fusion with metallic sodium. The resulting melt when dissolved in water and distilled with concentrated sulphuric acid gave a solution from which the fluorine could be precipitated as lead chlorofluoride. The phosphorus was always lost as phosphine.

Ruthenium and osmium. The first was generally determined by reducing the complex to the metal by heating in hydrogen, and sometimes by precipitating the dioxide by adding sodium carbonate to an aqueous solution of the compound. The gelatinous precipitate was separated, dried, and reduced in hydrogen to the metal. Each method gave consistent results which agreed with the other. Osmium was determined by reducing the preparation in hydrogen and allowing the metal to cool in a stream of carbon dioxide. In this way more than a trace of superficial oxidation was avoided.

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22. *Quinoxalines and Related Compounds. Part IV.* The Fine Structure of the 2- and 3-Hydroxyquinoxalines and 2-Amino- and 2-Mercapto-quinoxaline.*

By G. W. H. CHEESEMAN.

Ultraviolet absorption and ionisation properties indicate that 2- and 3-hydroxyquinoxalines exist in solution largely in the amide form. It is probable that in solution 2-aminoquinoxaline exists predominantly in the amino-form and 2-mercaptoquinoxaline in the thioamide form.

LITTLE is known about the ultraviolet absorption and ionisation properties of quinoxalines. In the present investigation the structures of the potentially tautomeric hydroxy-, amino-, and mercapto-quinoxalines have been studied by comparison of their ultraviolet spectra and ionisation constants with those of their fixed methylated tautomers.

The ultraviolet spectrum of the neutral molecule of 2-hydroxyquinoxaline was closely similar to that of its *N*-methyl derivative (I; R = Me, R_1 = H), but dissimilar from that of 2-methoxyquinoxaline (II; R = H) (Table, Fig. 1). This indicated that the hydroxy-compound existed largely in the amide form (I; R = R_1 = H). The cations of 2-hydroxy-quinoxaline and its *N*-methyl derivative also showed similar ultraviolet absorption; these spectra differed from the spectrum of the cation of 2-methoxyquinoxaline (Table, Fig. 2).

* Part III, *J.*, 1957, 3236.

Analogous relations were observed between the spectra of 2-hydroxy-3-methylquinoxaline and its *N*- and *O*-methyl derivatives both as neutral molecules and as cations (Table).

The relative basicities of these hydroxyquinoxalines and their *N*- and *O*-methyl derivatives (Table) also suggested that the hydroxy-compounds existed predominantly in the amide form. Thus the hydroxy-compounds were bases of similar strength to their *N*-methyl derivatives but appreciably weaker bases than their *O*-methyl derivatives. The

FIG. 1. *Neutral molecules of 2-hydroxy-* (——) *2-methoxy-* (. . . .), *and 1 : 2-dihydro-1-methyl-2-oxoquinoxaline* (– – – –).

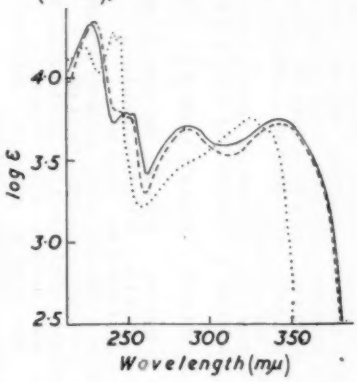
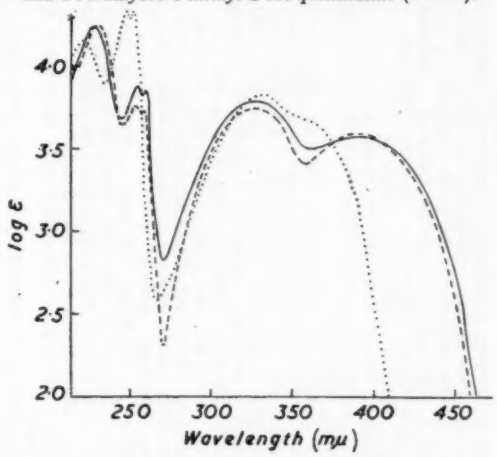
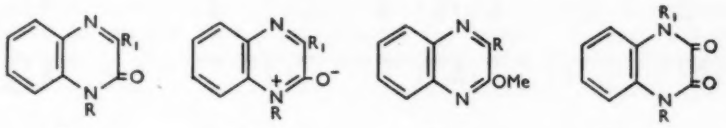


FIG. 2. *Cations of 2-hydroxy-* (——), *2-methoxy-* (. . . .), *and 1 : 2-dihydro-1-methyl-2-oxo-quinoxaline* (– – – –).



basic constants of 2-hydroxypyrazine (pK_a −0·1), its *N*-methyl derivative (pK_a −0·04), and 2-methoxypyrazine (pK_a 0·75) follow a similar pattern, and further examples may be cited.[1] The neutral molecules of the hydroxyquinoxalines and their *N*-methyl derivatives are stabilised by structures such as (Ia). There are however no similar resonance possibilities for base-weakening to stabilise the neutral molecules of the corresponding methoxyquinoxalines.



Oakes, Pascoe, and Rydon [2] compared the spectrum in ethanol of both 2 : 4-dihydroxy-1 : 3 : 5- and 2 : 4-dihydroxy-1 : 3 : 8-triaza-naphthalene with those of the *OO'*- and *NN'*-dimethyl derivatives. They concluded tentatively that these hydroxyazanaphthalenes exist as true hydroxy-compounds, but the *ON*-dimethyl derivatives were not available for comparison. It was therefore of interest to compare the spectrum of the neutral molecule of 2 : 3-dihydroxyquinoxaline with those of its *NN'*-, *ON*-, and *OO'*-dimethyl derivatives, (III; R = R_1 = Me), (I; R = Me, R_1 = OMe), and (II; R = OMe). The spectrum of the dihydroxy-compound most closely resembled that of its *NN*-dimethyl derivative (Table, Fig. 3), indicating that it must exist predominantly in the diamide form (III;

[1] Albert and Phillips, *J.*, 1956, 1294.
[2] Oakes, Pascoe, and Rydon, *J.*, 1956, 1045.

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Quinoxaline	Ionisation [a] (in H_2O) pK_a	Spread (±)	Concn. (10^{-5}M)	$\lambda_{analyt.}$ (mμ) [b]	Solv.[c]	Spectroscopy $\lambda_{max.}$, mμ ($\log_{10}\varepsilon$)
Parent	—	—	—	—	C_6H_{12} [d]	367(2·40) + 360(2·61) + 353(2·74) + 346(2·81) + 339(2·84); 316(3·80) + 310(3·69) + 304(3·74) + 298[e](3·63) + 293[e](3·59); 235(4·40) + 232(4·51) + 230—229[e](4·41)
2-Methyl-	—	—	—	—	,,	317(3·77) + 309—308(3·74) + 297[e](3·61); 238(4·38) + 234(4·48) + 231[e](4·38)
2-Chloro-	—	—	—	—	,,	329(3·68) + 319(3·795) + 311[e](3·73); 242(4·44) + 238(4·51) + 236—235[e](4·42)
2-Hydroxy-	—	—	—	—	H_2O 4·0 [f]	343(3·74); 287(3·70); 254(3·78) + 250(3·79); 228(4·32)
anion	9·12 [g]	0·03	250	—	H_2O 12·8	350(3·80); 288(3·31) + 282(3·30); 237(4·41)
cation	−1·38 [h]	0·01	6	390	H_2O −3·5	395—385(3·57—3·58); 326(3·79); 259(3·85) + 254(3·87); 228(4·25)
2-Methoxy-	—	—	—	—	C_6H_{12}	336(3·74) + 328(3·68) + 322(3·79) + 315(3·68) + 309(3·63); 278(3·49); 244(4·33) + 241(4·31); 225(4·28)
					EtOH	336(3·73) + 324(3·79) + 314(3·725); 288(3·55); 242(4·22); 223(4·22)
					H_2O 4·5	333[e](3·69) + 326(3·75); 245(4·25) + 241(4·26); 223(4·19)
cation	0·28	0·07	5	356	H_2O −3·3	353[e](3·70) + 331(3·84); 252(4·31) + 248(4·31); 222(4·14)
1 : 2-Dihydro-1-methyl-2-oxo-	—	—	—	—	C_6H_{12}	362—361(3·51) + 351(3·71) + 345(3·71) + 336(3·71) + 331[e](3·67) + 323[e](3·57); 290(3·60) + 286(3·55) + 279(3·73) + 270(3·61); 232(4·45)
					EtOH [i]	346(3·73) + 336(3·71); 282(3·73); 252[e](3·64) + 231(4·40)
					H_2O 4·5	345(3·715); 287(3·68); 252(3·76) + 245[e](3·80); 230(4·34)
cation	−1·15	0·04	6	391	H_2O −3·0	395—386(3·59—3·58); 326(3·74); 258(3·73) + 254(3·76); 231(4·24)
2-Hydroxy-3-methyl-	—	—	—	—	H_2O 4·0 [j]	340—330(3·83—3·84); 285(3·71); 254(3·79) + 250(3·79); 228(4·26)
anion	9·88	0·03	250	—	H_2O 12·8	343(3·90); 290(3·32); 238(4·40)
cation	0·48	0·04	5	375	H_2O −1·8	378—368(3·74); 320(3·795); 260(3·81) + 255(3·80); 230(4·23)
2-Methoxy-3-methyl-	—	—	—	—	C_6H_{12}	331(3·83) + 317(3·87) + 309(3·74); 244(4·30) + 240(4·29); 223[e](4·20)
					H_2O 5·1	332(3·81) + 319(3·88); 246(4·24) + 242—241(4·26); 223(4·17)
cation	1·38	0·01	5	350	H_2O −1·0	339(3·90); 252(4·305) + 248(4·27); 222(3·995)
1 : 2-Dihydro-1 : 3-dimethyl-2-oxo- [k]	—	—	—	—	C_6H_{12}	352[e](3·59) + 341(3·83) + 327—326(3·82); 288(3·66) + 277(3·81) + 270[e](3·75); 231 (4·48)
					H_2O 4·8	340—334(3·82—3·81); 285(3·71); 253(3·80) + 245[e](3·82); 228(4·30)
cation	0·51	0·09	5	375	H_2O −1·8	377—369(3·74); 316(3·77); 260(3·77) + 254(3·75); 231(4·22)
2 : 3-Dihydroxy- [l]	—	—	—	—	H_2O 5·1 [f]	342[e](3·68) + 326(4·00) + 312(4·07); 262[e](3·63) + 258(3·655); 236(3·90) + 229(4·00)
2 : 3-Dimethoxy-	—	—	—	—	C_6H_{12}	325(4·11) + 317(3·94) + 310(4·11) + 304(3·90) + 298—297(3·85) + 292—291(3·65) + 286(3·55) + 280(3·43) + 274(3·39); 243(4·26); 223[e](4·31)
					H_2O 5·1	325(3·91) + 311(3·99) + 301[e](3·81); 244(4·18); 222[e](4·21)
cation	−1·15	0·06	5	340	H_2O −3·3	336[e](3·99) + 329(4·01); 255(4·11) + 250(4·11); 225(4·06)
1 : 2-Dihydro-3-methoxy-1-methyl-2-oxo-	—	—	—	—	C_6H_{12}	334(3·73) + 322(3·97) + 310—309(3·92) + 290(3·66); 277(3·69) + 268—267(3·70) + 259(3·69); 230—229(4·28)
					H_2O 5·1	319(3·99) + 312[e](3·97); 252[e](3·87) + 248(3·88); 227(4·20)
1 : 2 : 3 : 4-Tetrahydro-1 : 4-dimethyl-2 : 3-dioxo-	—	—	—	—	H_2O 5·05	340[e](3·67); 325(3·99) + 313(4·05); 259[e](3·73) + 254(3·765); 238(4·01) + 232(4·06)
1 : 2-Dihydro-3-hydroxy-1-methyl-2-oxo-	—	—	—	—	EtOH	339[e](3·63) + 324(3·99) + 311(4·07) + 300[e](3·98); 259(3·71); 239(3·98) + 232—231 (4·025)
					H_2O 5·2	341[e](3·65) + 325(3·98) + 312(4·05); 261[e](3·66) + 256(3·695); 236[e](3·94) + 230(4·02)
anion	9·74	0·03	500	—	H_2O 12·8	338[e](3·90) + 325(4·11) + 314(4·07); 238(4·11)
2-Amino-	—	—	—	—	H_2O 7·2	353(3·80) + 310—290[e](3·39); 240(4·33)
cation	3·90 [m]	0·04	1000	—	H_2O 1·0	352—348(3·84) + 326—310[e](3·76); 257(4·07) + 252(4·05); 231(4·25)
2-Methylamino-	—	—	—	—	H_2O 7·2	363(3·79); 296—286[e](3·24—3·25); 248(4·43)
cation	4·10	0·05	1000	—	H_2O 1·0	354—350(3·855) + 312—304[e](3·74); 259(4·055) + 253(4·07) + 237(4·29)
2-Dimethylamino-	—	—	—	—	H_2O 7·2	382(3·845); 304—296[e](3·16—3·18); 254(4·40)
cation	3·72 [n]	0·02	1000	—	H_2O 1·0	368(3·93) + 320—314(3·72); 253[e](4·15) + 241(4·29)
2-Mercapto-	—	—	—	—	H_2O 3·8	405—395(4·04) + 329[e](3·37); 279(4·255)
anion	7·72 [o]	0·02	500		H_2O 11·65	382(3·92); 279(4·24); 217(4·23)
cation	−1·11	0·04	5	476	H_2O −3·3	480—476(3·86) + 400—360[e](3·36); 289(4·37)
2-Methylthio-	—	—	—	—	H_2O 4·9	356(3·94); 266(4·175); 240(4·16)
cation	0·26	0·06	5	391	H_2O −1·8	392(3·93); 257(4·20)

R = R_1 = H). The spectrum of the neutral molecule of 1 : 2-dihydro-3-hydroxy-1-methyl-2-oxoquinoxaline (I; R = Me, R_1 = OH) was closer to that of (III; R = R_1 = Me), its *N*-methyl derivative, than to that of (I; R = Me, R_1 = OMe), its *O*-methyl derivative (Table). Thus in common with other compounds with hydroxy-groups α to ring nitrogen atoms, the equilibrium for the tautomerism of the 2- and 3-hydroxyquinoxalines in solution is such that only small amounts of the enol form are present.[3]

Comparison of the spectra of the neutral molecules of 2-amino-, 2-methylamino-, and 2-dimethylamino-quinoxaline showed the expected bathochromic shifts of absorption bands associated with the substitution of a methyl group for the hydrogen atom of an amino-group (Table, Fig. 4).[4] The similarity in the spectra and ionisation constants of

FIG. 3. *Neutral molecules of* 2 : 3-*dihydroxy-* (——), 2 : 3-*dimethoxy-* (. . . .), 1 : 2-*dihydro*-3-*methoxy*-1-*methyl*-2-*oxo-* (— · — · —) *and* 1 : 2 : 3 : 4-*tetrahydro*-1 : 4-*dimethyl*-2 : 3-*dioxo-quinoxaline* (– – – –).

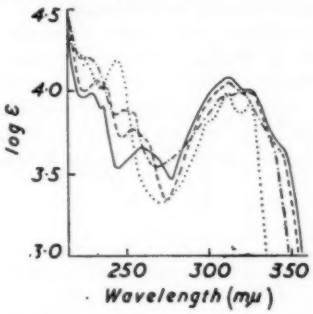
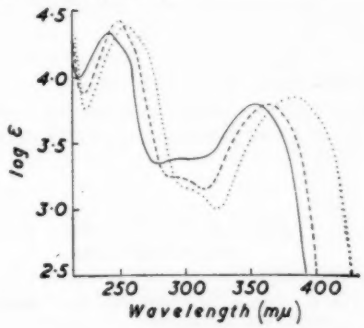


FIG. 4. *Neutral molecules of* 2-*amino-* (——), 2-*methylamino-* (– – – –), *and* 2-*dimethylamino-quinoxaline* (. . . .).



the 2-amino- and 2-dimethylamino-compounds suggested that 2-aminoquinoxaline existed predominantly in the amino- rather than the imino-form. This was to be expected, as related α-amino-*N*-heteroaromatic compounds have also been shown to exist mainly in the amino-form.[3] The evidence was incomplete as the corresponding nuclear *N*-methyl derivative of 2-aminoquinoxaline was not available for comparison. The change in spectrum which occurred when these aminoquinoxalines were dissolved in solutions sufficiently acid to convert them into mono-cations, indicated that it was a ring nitrogen, rather than the extranuclear nitrogen atom, that accepted the proton. However, Schofield and Osborn [5] have shown that 5-aminoquinoxaline accepts the first proton on the amino-group.

Footnotes to Table:

[a] Potentiometric determinations of p*K* were carried out at 25°, and spectroscopic determinations at room temperature, which varied from 15° to 25°. [b] An entry in this column indicates that the ionisation constant was determined spectroscopically. [c] Where the solvent was water the entry is followed by the pH of the solution. [d] Mason (*Chem. Soc. Special Publ.* No. 3, 1955, p. 139) gave $\lambda_{max.}$ 340 ($\log_{10}\varepsilon$ 2·76) and 312 (3·70). These values were taken from the smooth curve drawn through the vibrational fine structure of the n–π and first π–π bands. [e] Shoulder or inflection. [f] Spectrum in 0·1N-hydrochloric acid (Landquist, *J.*, 1953, 2830) showed similar $\lambda_{max.}$ and $\varepsilon_{max.}$ values. [g] Albert, Brown, and Cheeseman (*J.*, 1952, 1620) obtained 9·08 at 20°. [h] Albert and Phillips (*J.*, 1956, 1294) gave −1·37. [i] For spectrum in 96% ethanol, Clark-Lewis (*J.*, 1957, 422) gave $\lambda_{max.}$ 346 ($\log\varepsilon$ 3·72), 282 (3·72), and 230 (4·31). [j] Extinction curve by Lanning and Cohen (*J. Biol. Chem.*, 1951, **189**, 109) showed $\lambda_{max.}$ at *ca.* 335, 285, and 250 mμ. [k] For spectrum in ethanol, Dawson, Newbold, and Spring (*J.*, 1949, 2579) gave $\lambda_{max.}$ 336·5 ($\log_{10}\varepsilon$ 3·85), 280·5 (3·75), and 229 (4·33). [l] Albert and Phillips (*loc. cit.*) gave 9·52 for the acidic pK_a at 20°. [m] Albert, Goldacre, and Phillips (*J.*, 1948, 2240) obtained 3·96 at 20°. [n] In 10% ethanol. [o] In 50% ethanol.

[3] Albert, *Chem. Soc. Special Publ.* No. 3, 1955, p. 124.
[4] Brown and Short, *J.*, 1953, 331.
[5] Osborn and Schofield, *J.*, 1956, 4191.

The differences in the ultraviolet absorption spectra of the neutral molecules of 2-mercapto- and 2-methylthio-quinoxaline (Table, Fig. 5) suggested that the mercapto-compound existed mainly in the thioamide rather than the thiol form. There were also differences in the light absorption of the cations derived from these compounds (Table, Fig. 6). 2-Mercaptoquinoxaline proved to be a weaker base than its *S*-methyl derivative (Table). This again suggested a predominantly thioamide structure for 2-mercaptoquinoxaline, but more conclusive evidence must await measurements on the *N*-methyl derivative.

Quinoxalines, because of the 1 : 4-arrangement of their ring nitrogen atoms, are only weakly basic.[6] Methyl substitution has a base-strengthening effect, [*e.g.*, parent compound

FIG. 5. *Neutral molecules of 2-mercapto-* (——) *and 2-methylthio-quinoxaline* (. . . .).

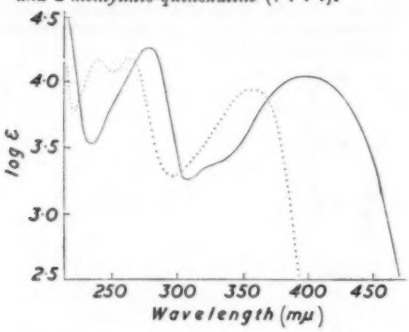


FIG. 6. *Cations of 2-mercapto-* (——) *and 2-methylthio-quinoxaline* . . . .).

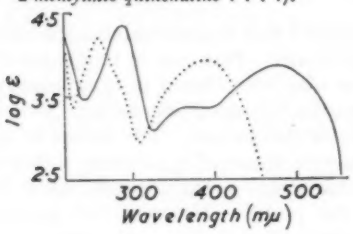
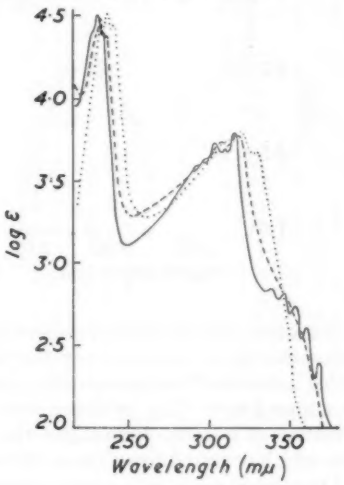


FIG. 7. *Spectrum of quinoxaline* (——), *2-methylquinoxaline* (– – – –), *and 2-chloroquinoxaline* (. . . .) *in* cyclo*hexane.*



(pK_a 0·56), 2-methylquinoxaline (pK_a 0·95) [7]. 2-Hydroxy-3-methylquinoxaline has now been found to be a stronger base than 2-hydroxyquinoxaline; the quinoxalines (I; R = R_1 = Me) and (II; R = Me) were similarly stronger bases than the corresponding demethyl compounds (I; R = Me, R_1 = H) and (II; R = H). Methoxyl substitution had a base-weakening effect, thus 2 : 3-dimethoxyquinoxaline was a weaker base than 2-methoxyquinoxaline, itself a weaker base than the parent compound. As expected 2-mercaptoquinoxaline was a stronger acid, and 3-methyl-2-hydroxyquinoxaline a weaker acid than 2-hydroxyquinoxaline.

The spectrum of quinoxaline in *cyclo*hexane (Table, Fig. 7) shows bands attributable to n–π and π–π transitions.[8a] In water [9] or methanol [10] the less intense n–π band is

[6] Albert, Goldacre, and Phillips, *J.*, 1948, 2240.
[7] Albert, Brown, and Wood, *J.*, 1954, 3832.
[8] Mason, (*a*) *Chem. Soc. Special. Publ.* No. 3, 1955, p. 139; (*b*) *J.*, 1955, 2336.
[9] Albert, Brown, and Cheeseman, *J.*, 1951, 474.
[10] Bohlmann, *Chem. Ber.*, 1951, **84**, 860.

obscured by the long-wave π–π band, since change from non-polar to polar solvent causes n–π bands to shift to shorter wavelengths, whereas π–π bands are not greatly affected by change of solvent.

Substitution in the quinoxaline nucleus at position 2 produces bathochromic shifts in the π–π bands. This increases in the order Me < Cl < OMe < SMe < NMe_2 (Table, Fig. 7). These substituents produce similar bathochromic effects on the 260 mμ band of the benzene spectrum and the 300 mμ band of the pteridine spectrum.[8b] By analogy with the spectra of the chloropyrazines[11] and chloropteridines,[8b] a chloro-substituent should exert a hypsochromic effect on the n–π band of the quinoxaline spectrum. This effect was not observed in the spectrum of 2-chloroquinoxaline in *cyclo*hexane (Table, Fig. 7) because the n–π band was obscured by the more intense π–π band. A comparison of the spectra of 2-methoxy-, 2-methoxy-3-methyl-, and 2 : 3-dimethoxy-quinoxaline in water or *cyclo*hexane indicated that the long-wave band of the disubstituted quinoxalines was of increased intensity but at slightly shorter wavelengths.

The anomalous features in the spectrum of the neutral molecule of 6-hydroxypteridine, the pteridine analogue of 2-hydroxyquinoxaline, are due to the formation of a hydrate, the molecule of water being added across the 7 : 8-carbon–nitrogen double bond.[12] No similar anomalies were observed in the spectrum of the neutral molecule of 2-hydroxyquinoxaline. On anionisation a bathochromic shift characteristic of the hydroxyazanaphthalenes was observed (Table).[12] The spectrum of the anion of 2-hydroxyquinoxaline resembled that of the neutral molecule of 2-aminoquinoxaline, as is general for phenoxide ions and the corresponding aromatic amines.[13]

Experimental

Materials.—Quinoxaline and 2-methylquinoxaline were prepared by Jones and McLaughlin's method.[14] The sources of other quinoxalines were given in earlier papers.[15]

Physical Measurements.—Ultraviolet measurements were made with a Unicam S.P. 500 instrument. Measurements of pH were made with a Cambridge bench-type pH meter, standardised with buffer solutions of pH 4·00 and 9·19 at 25°, prepared from Cambridge buffer tablets. A Doran Alkacid sealed glass electrode and a Cambridge calomel electrode were used. Glycine, acetate, and phosphate buffers (0·01M) were used; solutions of lower pH were prepared from standard solutions of either hydrochloric or sulphuric[16] acid. Ionisation constants were determined either potentiometrically or spectroscopically in the usual manner.[1] The limits quoted in the table define the spread in the calculated pK_a values over the range 30—70% neutralisation.

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[11] Halverson and Hirt, *J. Chem. Phys.*, 1951, **19**, 711.
[12] Brown and Mason, *J.*, 1956, 3443.
[13] Jones, *J. Amer. Chem. Soc.*, 1945, **67**, 2127.
[14] Jones and McLaughlin, *Org. Synth.*, 1950, **30**, 86.
[15] Cheeseman, (*a*) *J.*, 1955, 1804; (*b*) *J.*, 1957, 3236.
[16] Michaelis and Granick, *J. Amer. Chem. Soc.*, 1942, **64**, 1861.

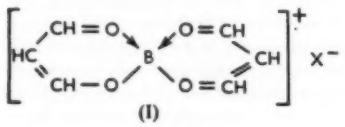
XUM

23. *The Existence of an Organic Cation containing Boron.*

By J. M. Davidson and C. M. French.

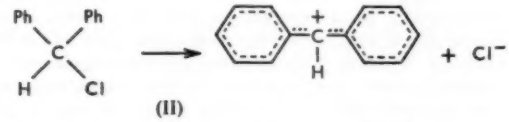
The ultraviolet absorption spectrum of a solution in ethyl methyl ketone of diphenylboron chloride containing 1 equiv. of aluminium trichloride has been compared with that of a solution in the same solvent of diphenylmethyl bromide and aluminium trichloride. The close agreement between the positions of the maxima of the two curves, and the agreement with the value predicted from molecular-orbital calculations for the diphenylboronium ion indicate the presence of this ion in the coloured ketone solution. Further evidence for this is adduced from conductivity measurements on solutions of diphenylboron chloride and aluminium trichloride separately and together in nitrobenzene, and from the ready reaction between the boron compound and silver perchlorate to precipitate silver chloride.

The only known cations which contain boron are the boronium salts obtained by Dilthey and Schumacher,[1] and these are chelate complexes of the type (I). In general the electronic structure of the boron atom precludes the existence of a positive centre of charge on it. The present work concerns the formation of boronium ions exactly analogous to the well-known carbonium ions. Cations of tervalent carbon invariably exist in a state which is stabilised by conjugation energy, or occasionally by release of steric hindrance. Thus aryl-substituted methyl chlorides ionise readily in polar solvents, to form a coloured cation. In solvents with readily available lone pairs of electrons, *e.g.*, ketones and nitrobenzene, compounds of the diarylboron chloride type will be solvated, and the boron atom will become isoelectronic with the central carbon atom of the arylmethyl chlorides [cf. (II) and (III)]. We have shown that in an ionising solvent diphenylboron chloride ionises to form the diphenylboronium ion.



(I)

(IV)



(II)

(III)

Diphenylboron chloride prepared by Abel, Dandegaonker, Gerrard, and Lappert's method [2] was dissolved in dry ethyl methyl ketone to form a colourless solution which had an equivalent conductance of $\Lambda = 3{\cdot}79 \times 10^{-2}$ ohm^{-1} cm.^{2} at a concentration of 0·0356M (all conductivity measurements were made at 15°). However, a solution in ethyl methyl ketone of equivalent amounts of the same halide and of aluminium trichloride, which was added to induce ionisation of the boron–chlorine linkage, was bright yellow and had $\Lambda =$ 36·6 ohm^{-1} cm.^{2} at 0·047M. Using a similar solution of concentration 0·022M, we recorded the ultraviolet absorption on " Unicam " spectrophotometer, and compared the spectrogram with that of a 0·006M solution of diphenylmethyl bromide similarly mixed with 1 equiv. of aluminium trichloride in ethyl methyl ketone (Fig. 1). In view of the concentrated solutions used, the actual intensity of absorption in 1 cm. cells represents too low a degree of ionisation to permit calculation of the extinction coefficients.

[1] Dilthey and Schumacher, *Annalen*, 1906, **344**, 300, 326.
[2] Abel, Dandegaonker, Gerrard, and Lappert, *J.*, 1956, 4697.

The maxima at 337 mμ for the diphenylboronium ion, and 327 mμ for the diphenylmethyl cation, qualitatively agree well from the point of view of the identity of the former system. The colour of both these cations may be considered as due to the isoelectronic π-electron systems in the odd-alternant cations (IV).

The boron compound system comprises twelve carbon $2p$ orbitals and one boron $2p$ orbital, and the conjugated system will have six filled bonding molecular orbitals, six antibonding ones, and one non-bonding one, all of which will be unfilled. Let Ψ be the

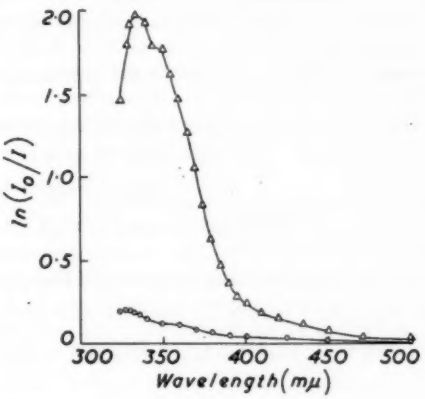


FIG. 1.
△ Ph_2BCl–$AlCl_3$.
○ Ph_2CHBr–$AlCl_3$.

wave function of one of the bonding molecular orbitals of energy E. The first absorption band will be due to the transition between this orbital and the non-bonding orbital which will have the same energy as a carbon $2p$ orbital, and may be taken as an arbitrary zero,[3]

$$H\Psi = E\Psi$$

where H is the Hamiltonian operator for the system. Now the above alternant system can be divided into three odd-alternant systems so that it becomes a linear combination of these three:

$$\Psi = C_1\psi_1 + C_2\psi_2 + C_3\psi_3$$

The secular equation derived from the perturbation treatment can be written down at once:

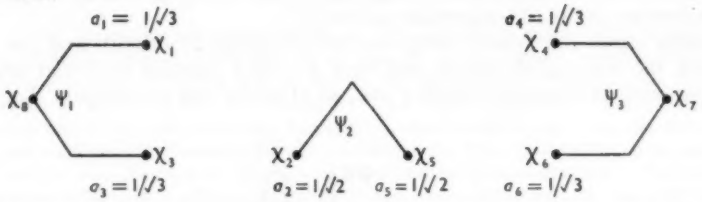
$$\begin{vmatrix} (\int\psi_1 H\psi_1 d\tau - & \int\psi_1 H\psi_2 d\tau & \int\psi_1 H\psi_3 d\tau \\ \int\psi_2 H\psi_1 d\tau & (\int\psi_2 H\psi_2 d\tau - E) & \int\psi_2 H\psi_3 d\tau \\ \int\psi_3 H\psi_1 d\tau & \int\psi_3 H\psi_2 d\tau & (\int\psi_3 H\psi_3 d\tau - E) \end{vmatrix} = 0$$

However, the three molecular orbitals can now be further expanded as a linear combination

[3] Dewar, *J.*, 1952, 3532.

of atomic orbitals in which the distribution coefficients can be written down at sight, for:[4]

$\Sigma(a_{oi})^2 = 1$



The molecular orbitals of the alternant systems are a linear combination of these atomic orbitals, *i.e.*,

$$\psi_1 = a_1\chi_1 + a_3\chi_3 + a_8\chi_8$$
$$\psi_2 = a_2\chi_2 + a_5\chi_5$$
$$\psi_3 = a_4\chi_4 + a_6\chi_6 + a_7\chi_7$$
$$\therefore \int\psi_1 H\psi_2 d\tau = a_1a_2\int\chi_1 H\chi_2 d\tau + a_3a_2\int\chi_3 H\chi_2 d\tau \ldots \text{ etc.}$$

This expansion omits all integrals in which the χ's do not overlap. However, the χ wave functions are merely carbon $2p$ orbitals, and so $\int\chi_1 H\chi_2 d\tau = \beta$ where β is the resonance integral. Similarly $\int\chi_1 H\chi_1 d\tau = \alpha$ where α is the Coulomb integral. Now $(\alpha - E) = x$

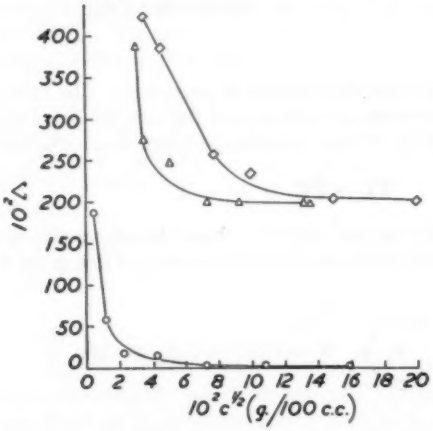


FIG. 2.
○ Ph_2BCl.
◇ $AlCl_3$.
△ Ph_2BCl–$AlCl_3$.

where x represents the energy interval between the conjugated system and the non-bonding molecular oblital, which is the energy associated with the first absorption band. Hence

$$\begin{vmatrix} x & \left(\frac{1}{\sqrt{3}\sqrt{2}} + \frac{1}{\sqrt{3}\sqrt{2}}\right)\beta & 0 \\ \left(\frac{1}{\sqrt{3}\sqrt{2}} + \frac{1}{\sqrt{3}\sqrt{2}}\right)\beta & x & \left(\frac{1}{\sqrt{3}\sqrt{2}} + \frac{1}{\sqrt{3}\sqrt{2}}\right)\beta \\ 0 & \left(\frac{1}{\sqrt{3}\sqrt{2}} + \frac{1}{\sqrt{3}\sqrt{2}}\right)\beta & x \end{vmatrix} = \begin{vmatrix} x & \beta\sqrt{\frac{2}{3}} & 0 \\ \beta\sqrt{\frac{2}{3}} & x & \beta\sqrt{\frac{2}{3}} \\ 0 & \beta\sqrt{\frac{2}{3}} & x \end{vmatrix}$$

Therefore $x = 2\beta/\sqrt{3}$.

But $x = h\nu$, and therefore $hc/\lambda = 2\beta/\sqrt{3}$.

[4] Dewar, *J. Amer. Chem. Soc.*, 1952, **74**, 3341 *et seq.*

The wavelength λ of the first absorption band for benzene is 208 mμ for a transition of energy 2β. Hence

$$hc/208 = 2\beta;\ hc/\beta = 416;\ \lambda = 416 \times 3^{1}/2 = 360\ \text{m}\mu$$

This value of 360 mμ is in very fair agreement with the observed values.

Attempts to study the electrochemistry of the diphenylboronium ion in ethyl methyl ketone solution have not been successful, as the solvent cannot be adequately dried for a conductance run involving low concentrations. The reason for this is that even very small traces of water in the solvent result in the diphenylboron chloride's becoming more hydrolysed as solvent is added in successive dilutions, and the resulting hydrogen chloride interferes. Conductance measurements in dry nitrobenzene were more successful, and the conductance of diphenylboron chloride in this solvent is shown in Fig. 2. An accurate estimate of Λ_0 has not been obtained, but assuming $\Lambda_0 = 25{\cdot}0$ to be a typical value for weak electrolytes in this solvent, and taking Λ/Λ_0 as an approximate measure of the degree of ionisation, we find that the latter is much less than 1% at the higher concentrations used here.

A solution of equivalent amounts of diphenylboron chloride and aluminium trichloride is darker in colour than the pure solvent, and a comparison of the conductivity curve for this system with that of aluminium trichloride alone in nitrobenzene shows the interaction of the two halides. Although aluminium trichloride itself is a weak electrolyte, in dilute solution, at least, the conductivity of a system containing solvated diphenylboronium ions and $AlCl_4^-$ ions should be lower, as these large ions should have lower mobilities, and thus lower equivalent conductivities. At higher concentrations however, the degree of ionisation of the salt having the larger ions should be greater than that of aluminium trichloride, and hence the two curves should at least approach each other, as is the case.

Despite the very low apparent degree of dissociation of diphenylboron chloride in nitrobenzene, metathesis takes place with silver perchlorate, and silver chloride is precipitated at once. After filtration the solution contains diphenylboron perchlorate (Ph_2BClO_4), and such a solution made up to 0·03M had an equivalent conductance of $\Lambda = 3{\cdot}4$ ohm^{-1} cm.^{2}, which is very similar to the value for $(Ph_2B^+)(AlCl_4^-)$ and is evidence for the existence of the same cation in both solutions.

We could not precipitate a solid perchlorate by addition of other organic solvents such as dry ether, carbon tetrachloride, etc., to the nitrobenzene solution.

Experimental

Nitrobenzene was fractionated over phosphoric oxide; the middle fraction was kept over baked-out activated alumina for three days with intermittent shaking, then filtered off in a dry box (b. p. 54°/0·13 mm.; n_D^{20} 1·5519; d_4^{15} 1·2082; specific conductivity at 15°, 9×10^{-9} ohm^{-1} cm.$^{-1}$).

" AnalaR " ethyl methyl ketone was fractionated, and after the fore-run had been neglected, the fraction of b. p. 79·2°/760 mm. was collected and further dried by refluxing over baked-out activated alumina (n_D^{20} 1·3760; d_4^{15} 0·8100).

Aluminium trichloride was repeatedly sublimed first at atmospheric pressure and then *in vacuo*, with a sublimator that was loaded and unloaded in an atmosphere of nitrogen in a dry-box.

All solutions were made up in the dry-box.

Conductivity measurements were made by using the a.c. bridge technique and apparatus.[5]

The authors thank Mr. D. S. Urch for helpful discussion. One of them (J. M. D.) thanks the British Thomson-Houston Co. Ltd. for a Research Scholarship.

Chemistry Department, Queen Mary College, Mile End Road,
London, E.1. [*Received, August 13th*, 1957.]

[5] French and Glover, *Trans. Faraday Soc.*, 1955, **51**, 1418.

XUM

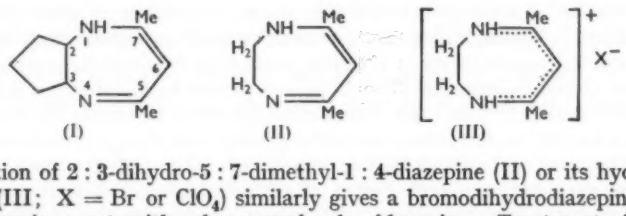
24. *Diazepines. Part II.* Some Bromination Experiments on Dihydrodiazepines.*

By Douglas Lloyd and Donald R. Marshall.

The bromination of two 2 : 3-dihydro-1 : 4-diazepines has been studied. One bromine atom only enters the molecule, by substitution, at the 6-position. This bromine atom is easily replaced by a methoxy- or ethoxy-group.

The preparation is recorded of a number of 2 : 3-benzo-1 : 4-diazepines [1] and 2 : 3-dihydro-1 : 4-diazepines,[2] but little systematic investigation of their chemical properties has been carried out, especially in the case of the dihydrodiazepines. As the first stage of an investigation of their properties, the bromination products derived from two 2 : 3-dihydro-5 : 7-dimethyl-1 : 4-diazepines have been studied.

If 2 : 3-dihydro-5 : 7-dimethyl-2 : 3-*cyclo*pentano-1 : 4-diazepine (I) is treated with an equimolecular portion of bromine, an almost colourless product crystallises at once. More bromine will not react, even over a period of four days. The product contains two atoms of bromine, one of which is ionic, and is apparently a bromodihydrodiazepinium bromide.



(I) (II) (III)

Bromination of 2 : 3-dihydro-5 : 7-dimethyl-1 : 4-diazepine (II) or its hydrobromide or perchlorate (III; X = Br or ClO_4) similarly gives a bromodihydrodiazepinium bromide; again the diazepine reacts with only one molecule of bromine. Treatment of the resultant bromide with sodium hydroxide solution yields the corresponding bromodihydrodiazepine base. Bromination by *N*-bromosuccinimide gives the same product as is obtained by using bromine.

As only one bromine atom enters the molecule, it must presumably do so at a unique position, namely the 6-position. This is confirmed by the hydrolysis products obtained when the bromo-compound is kept in dilute sulphuric acid for some days. A lachrymatory oil separates, which contains bromine but no nitrogen. This oil shows acidic or enolic properties and with ferric chloride gives an intense purple colour. It has been pointed out [3] that α-substituted β-dicarbonyl compounds give violet, purple, or blue colours with ferric chloride: of all the simple β-dicarbonyl compounds listed in Beilstein's " Handbuch " those giving blue or purple colours with this reagent are indeed all α-substituted. It is likely therefore that the oil is 3-bromoacetylacetone. When the aqueous layer from the hydrolysis is basified, benzoyl and toluene-*p*-sulphonyl derivatives can be obtained from it which are identical (mixed m. p.) with those obtained from ethylenediamine. These hydrolysis products could only arise from 6-bromo-2 : 3-dihydro-5 : 7-dimethyl-1 : 4-diazepine.

Treatment of this 6-bromo-compound with potassium methoxide or ethoxide readily gives products which are apparently 6-methoxy- and 6-ethoxy-2 : 3-dihydro-5 : 7-dimethyl-1 : 4-diazepine respectively, as indicated by their molecular formulæ. That the

* Part I, *J.*, 1956, 2597.

[1] Thiele and Steimmig, *Ber.*, 1907, **40**, 955; Rupe and Huber, *Helv. Chim. Acta*, 1927, **10**, 846; Emmert and Gsottschneider, *Ber.*, 1933, **66**, 1871; Vaysman, *Trudy Inst. Khim. Khar'kov Gosudarst. Univ.*, 1938, **4**, 157; 1940, **5**, 57; Schmitt, *Annalen*, 1950, **569**, 17; Haley and Maitland, *J.*, 1951, 3155; King and Spensley, *J.*, 1952, 2144; Ried and Höhne, *Chem. Ber.*, 1954, **87**, 1801.

[2] Schwarzenbach and Lütz, *Helv. Chim. Acta*, 1940, **23**, 1139; Ried and Höhne, *Chem. Ber.*, 1954, **87**, 1811; Lloyd and Marshall, *J.*, 1956, 2597.

[3] Morgan and Drew, *J.*, 1924, **125**, 731; Henecka, *Chem. Ber.*, 1948, **81**, 179.

alcoholic alkali has brought about substitution, and not elimination producing compounds which with alcohol of crystallisation would have the same formulæ, is shown in that the picrates of these compounds are unchanged by acetic acid and acetic anhydride. The similarity of their ultraviolet spectra to that of the bromodihydrodiazepine also confirms this formulation.

Introduction of a bromine atom or alkoxy-group into the dihydrodiazepines causes little change in the general form of the spectra but there is a bathochromic displacement (about 24 mμ) of the main peak, this again being consistent with the structures assigned.

Experimental

2 : 3-Dihydro-5 : 7-dimethyl-2 : 3-*cyclo*pentano-1 : 4-diazepine (I) and 2 : 3-dihydro-5 : 7-dimethyl-1 : 4-diazepine (II) were prepared as described in Part I.

Bromination of the Diazepine (I).—Treatment of an ethereal solution of this base (0·33 g.) with an equimolar quantity of bromine gave an immediate precipitate of *6-bromo-2 : 3-dihydro-5 : 7-dimethyl-2 : 3-cyclopentano-1 : 4-diazepinium bromide* as pale yellow needles (0·54 g., 83%) which, recrystallised from water or ethanol, darken above 190°, fusing with decomposition at 360—370°. They are moderately soluble in water, less soluble in methanol or ethanol, insoluble in acetone, ether, chloroform, and carbon tetrachloride; the aqueous solution gives a halide reaction with silver nitrate (Found: C, 37·4; H, 5·1; N, 8·8; Br, 48·4. $C_{10}H_{14}N_2Br_2$ requires C, 37·0; H, 4·9; N, 8·6; Br, 49·4%).

Bromination of the Diazepine (II).—A solution of this base (4·3 g.) in dry ether was treated with bromine until no more solid was precipitated. This solid, recrystallised from ethyl acetate–methanol as yellow needles, m. p. 207—208° (5·9 g., 60%), was 6-bromo-2 : 3-dihydro-5 : 7-dimethyl-1 : 4-diazepinium bromide. Treatment of this in water with excess of sodium hydroxide gave *6-bromo-2 : 3-dihydro-5 : 7-dimethyl-1 : 4-diazepine*, m. p. 122—123° (Found: C, 41·6; H, 5·4; N, 13·7; Br, 39·1. $C_7H_{11}N_2Br$ requires C, 41·4; H, 5·4; N, 13·8; Br, 39·4%). This base forms a *perchlorate*, pale yellow needles (from water), m. p. 161—162°, sparingly soluble in methanol and ethanol, soluble in water and acetone (Found: C, 28·8; H, 4·1; N, 9·8; Hal, 38·2. $C_7H_{12}O_4N_2BrCl$ requires C, 27·7; H, 4·0; N, 9·2; Hal, 38·1%), and a *picrate*, m. p. 207—209° (Found: C, 36·3; H, 3·2; N, 16·0; Br, 17·9. $C_{13}H_{14}O_7N_5Br$ requires C, 36·1; H, 3·2; N, 16·2; Br, 18·5%). The hydrochloride or perchlorate of the starting material was also readily brominated in chloroform or methanol, to give the 6-bromo-derivative (90%).

Bromination with N-Bromosuccinimide.—The perchlorate of the base (II) (2·24 g., 0·010 mole) and *N*-bromosuccinimide (2·0 g., 0·011 mole) in chloroform were heated under reflux for 2 hr. The bromodihydrodiazepinium perchlorate separated from the solution mixed with succinimide. Recrystallised from water it had m. p. 161—162° (1·86 g., 61%).

Acid Degradation of the Bromodihydrodiazepine from (II).—The base (9·0 g.) was added to 2N-sulphuric acid and kept for 5 days. An oil (6 g.) separated which was lachrymatory, dissolved in aqueous sodium hydroxide, contained bromine but no nitrogen, and gave an intense purple colour with ferric chloride solution. With Brady's reagent it gave an orange gum. The residual acid solution was extracted with ether and made alkaline with sodium hydroxide, and portions were shaken with benzoyl chloride and toluene-*p*-sulphonyl chloride severally. The dibenzoyl (m. p. 252—253°) and ditoluene-*p*-sulphonyl (m. p. 161—162°) derivatives of ethylenediamine were formed. These m. p.s were not depressed on admixture with genuine samples. In another hydrolysis 2·0 g. of the bromo-base gave 2·4 g. of dibenzoylethylenediamine (91%).

6-Ethoxy-2 : 3-dihydro-5 : 7-dimethyl-1 : 4-diazepine.—Potassium hydroxide (4 g.) in ethanol (30 ml.) was added to a solution of the bromodihydrodiazepinium bromide (5 g.) in ethanol (30 ml.), and the mixture heated under reflux for 30 min. and then kept overnight. Potassium bromide (4·08 g., 97%) was filtered off, and the solution acidified with concentrated hydrobromic acid, filtered, and evaporated to dryness *in vacuo*. The residue was dissolved in 10% aqueous sodium hydroxide (50 ml.) and this solution extracted with ether (6 × 20 ml.). Removal of ether from the extract gave a brown gum which crystallised. It is soluble in many organic solvents, but not light petroleum or benzene, and gives a *picrate*, m. p. 167·5—168·5° (from ethanol) (Found: C, 44·8; H, 4·8; N, 17·2. $C_{15}H_{19}O_8N_5$ requires C, 45·3; H, 4·8; N, 17·6%). This picrate was also obtained by refluxing the bromo-hydrobromide from (III; X = Br) with ethanolic alkali and adding picric acid directly

2 : 3-*Dihydro*-6-*methoxy*-5 : 7-*dimethyl*-1 : 4-*diazepine*.—The bromodihydrodiazepine (6·44 g.) and potassium hydroxide (2·15 g.) in methanol (30 ml.) were heated under reflux for 2 min. After cooling and removal of the precipitated potassium bromide, picric acid (10·6 g.) in boiling methanol (60 ml.) was added. The hot solution was filtered from potassium picrate, and the *methoxydihydrodiazepinium picrate* which separated recrystallised from methanol; it had m. p. 157—159° (Found: N, 17·6. $C_{14}H_{17}O_8N_5$ requires N, 18·3%). This picrate and that of its ethoxy-analogue were unchanged when heated with acetic acid–acetic anhydride.

Ultraviolet spectra (*in* MeOH).

2 : 3-Dihydro-5 : 7-dimethyl-1 : 4-diazepinium derivative	$\lambda_{max.}$ (mμ)	log ε	2 : 3-Dihydro-5 : 7-dimethyl-1 : 4-diazepinium derivative	$\lambda_{max.}$ (mμ)	log ε
Cation (III)	325	4·3	6-Methoxy-	349, 256	4·3, 3·1
2 : 3-*cyclo*Pentano- (in H_2O)...	325	4·2	6-Ethoxy-	352, 256	4·2, 2·9
6-Bromo-	349, 260	4·1, 3·0			

We are indebted to the Department of Scientific and Industrial Research for financial assistance (to D. R. M.).

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25. *Some Derivatives of* tert.-*Butylbenzene.*

By F. BELL.

Space-filling atomic models can represent only with difficulty 2 : 6-disubstituted *tert.*-butylbenzenes, particularly if the substituents are halogen atoms. In the present paper a number of such compounds, *e.g.*, (V)—(VII), are described and their ready formation reflects clearly on the limitations of these models.

Further examples are provided of the displacement of a *tert.*-butyl group from the benzene nucleus during substitution experiments.

MANY have directed attention to steric hindrance effects associated with a *tert.*-butyl group in the benzene nucleus but little regard has been paid to the surprising *ease* with which substituents can be introduced into both of the positions *ortho* to this group. The papers of Carpenter, Easter, and Wood are rich in illustrations of this type of reaction. They have shown that a nitro-group can be introduced into position 6 of a *tert.*-butylbenzene with NO_2, Me, Pr^i, NH_2, CN, OMe, or CHO already in position 2. With some types of space-filling models it is just possible to construct these molecules, but such models are unable to represent compound (I), which has been prepared both by Carpenter and Easter [1] and by Burgoyne, Klose, and Watson.[2] The aim of the present research was to prepare further examples of this stereochemically interesting type of compound.

First, use was made of the readily available 4-*tert.*-butyl-2 : 6-dinitrotoluene [3] to prepare 2-amino-6-nitro- and 2 : 6-diamino-4-*tert.*-butyltoluenes and their acetyl and toluene-*p*-sulphonyl derivatives. It was found that 3-*tert.*-butyl-6-methyl-5-nitro-*N*-toluene-*p*-sulphonylaniline (II) could be only monochlorinated and monobrominated; the diamide (III), also, could be only monobrominated but both the diamides (III) and (IV) were readily dichlorinated at the vacant positions.

Next it was found that 1 : 4-dibromo-2 : 5-di-*tert.*-butylbenzene [4] could be mononitrated. The product (V) is a compound of the desired type. Attempts to convert it into the amine were unsuccessful. 1 : 4-Di-*tert.*-butyl-2 : 5-di-iodobenzene, prepared from

[1] Carpenter and Easter, *J. Org. Chem.*, 1954, **19**, 77.
[2] Burgoyne, Klose, and Watson, *ibid.*, 1955, **20**, 1508.
[3] Brady and Lahiri, *J.*, 1934, 1954.
[4] Kofod, Kumar, and Sutton, *J.*, 1951, 1793.

1 : 4-diamino-2 : 5-di-*tert.*-butylbenzene, with nitric acid gave in fairly good yield 2 : 5-di-*tert.*-butyl-4-iodonitrobenzene, an iodine atom and not, as is usual in this series, a *tert.*-butyl group having undergone displacement. 1 : 4-Diamino-2 : 5-di-*tert.*-butylbenzene was converted by bromine in acetic acid into 2 : 5-di-*tert.*-butylbenzoquinone, but with *N*-bromosuccinimide in pyridine gave 2 : 5-di-*tert.*-butylbenzoquinone dibromodi-imide.

4-*tert.*-Butyl-3 : 5-dinitrobenzoic acid [5] was reduced to 3-amino-4-*tert.*-butyl-5-nitrobenzoic acid in good yield and from this diazo-reactions smoothly gave acids (VI) and (VII), which formed soluble sodium salts. Both these halogenated acids rapidly became red on exposure to light. An attempt was made to prepare the acid (VI) from 3-bromo-4-*tert.*-butylbenzoic acid (VIII), obtained by the bromination of 4-*tert.*-butylbenzoic acid; since this bromo-acid was not easily decarboxylated, it was oriented by conversion by the Hofmann reaction into the amine, whose acetyl derivative [6] (IX) is readily distinguished from the isomer (X) obtained in almost quantitative yield by bromination of 4-*tert.*-butylacetanilide.[7] The bromo-acid (VIII), on treatment with fuming nitric acid, gave two mononitro-derivatives, neither identical with (VI). Both yielded sparingly soluble sodium salts and were not particularly sensitive to light. Attempts to brominate 2- and 3-nitro-4-*tert.*-butylbenzoic acid either by bromine and an iron catalyst or by Derbyshire and Waters's method [8] were unsuccessful. The *tert.*-butyl-nitrobenzoic acids offer a ready source of *tert.*-butyl-nitrobenzenes and *tert.*-butyl-2 : 5- and -2 : 6-dinitrobenzenes are described in the Experimental part.

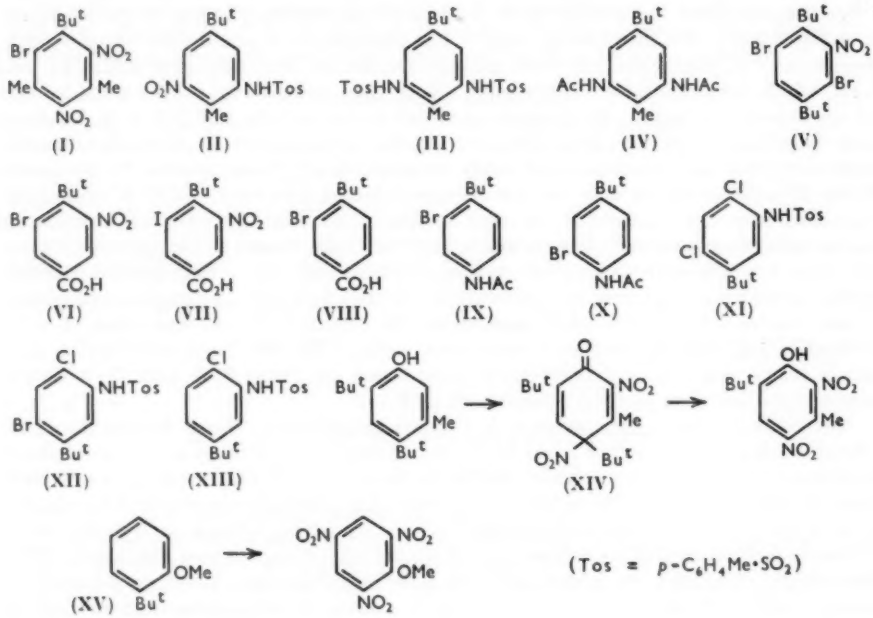
Next were examined derivatives of 2 : 5-di-*tert.*-butylaniline. Both the acetyl and the toluene-*p*-sulphonyl derivative could be monochlorinated. Continued action of sulphuryl chloride on the toluene-*p*-sulphonyl derivative resulted in displacement of a *tert.*-butyl group by chlorine to give the dichloro-compound (XI), alternatively prepared by chlorination of 3-*tert.*-butyl-*N*-toluene-*p*-sulphonylaniline. Similarly 4-bromo-2 : 5-di-*tert.*-butyl-*N*-toluene-*p*-sulphonylaniline suffered loss of a *tert.*-butyl group to give the amide (XII), alternatively prepared by bromination of 5-*tert.*-butyl-2-chloro-*N*-toluene-*p*-sulphonylaniline (XIII). 2 : 4-Dibromo-5-*tert.*-butyl-*N*-toluene-*p*-sulphonylaniline suffered no change with sulphuryl chloride.

Many examples are now known of the removal of the *tert.*-butyl group from the benzene nucleus in the course of substitution experiments and, indeed, the poor yields obtained in many simple reactions, *e.g.*, the less than 40% yield now recorded for the conversion of 4-*tert.*-butyl-2-nitroacetanilide into the dinitro-derivative, is in the main occasioned by side reactions involving displacement of the *tert.*-butyl group. The examples fall into two classes: (*a*) removal under the action of a reagent such as aluminium chloride [9] or hydrogen fluoride,[10] leaving hydrogen in the vacated position; and (*b*) removal by nitric acid,[11] bromine,[12] or sulphuryl chloride with entry of NO_2, Br, or Cl respectively. In class (*b*) the replacement is favoured by the presence of a powerfully *ortho-para*-directing group, such as OH, OMe, or $NH{\cdot}SO_2{\cdot}C_7H_7$, in the *ortho*- or *para*-position to the *tert.*-butyl group, and various mechanisms are possible. Robertson [13] has suggested that the *tert.*-butyl group separates as a positive ion; in other examples it has been possible to isolate quinonoid intermediates, *e.g.*, (XIV), which readily pass into the final products by expulsion of butylene. In others, *e.g.*, (XV), it appears probable that the replacement involves

[5] Bell, *J.*, 1956, 3243.
[6] Shoesmith and Mackie, *J.*, 1928, 2339.
[7] Crawford and Stewart, *J.*, 1952, 4447; Cadogan, Hey, and Williams, *J.*, 1954, 3357; de la Mare and Harvey, *J.*, 1957, 131.
[8] Derbyshire and Waters, *J.*, 1950, 573.
[9] Kulka, *J. Amer. Chem. Soc.*, 1954, **76**, 5469.
[10] Schlatter, *ibid.*, p. 4952.
[11] Albert and Sears, *ibid.*, p. 4979; Carpenter, Easter, and Wood, *J. Org. Chem.*, 1951, **16**, 586; Bell and Wilson, *J.*, 1956, 2340.
[12] Muller, Ley, and Kiedaisch, *Chem. Ber.*, 1954, **87**, 1605; Forman and Sears, *J. Amer. Chem. Soc.*, 1954, **76**, 4977; Bartlett, Roha, and Stiles, *ibid.*, p. 2349.
[13] Robertson, *Science Progr.*, 1955, 431.

XUM

formation of a transition complex under the action of the *ortho-para*-directing group, followed by abstraction of a proton from the *tert.*-butyl group, which is then expelled as butylene.



Bartlett, Roha, and Stiles [12] obtained, by bromination of 2 : 5-di-*tert.*-butylaniline, a dibromo-derivative, which crystallised from ethanol in pale pink prisms, m. p. 256° (decomp.). This would of necessity be the 4 : 6-dibromo-compound, in which a *tert.*-butyl group is flanked by two bromine atoms. Repetition of this experiment gave the readily soluble monobromo-derivative, m. p. 90°, and its hydrobromide together with a very small yield of a compound which was only slightly soluble in the ordinary organic solvents even at the boiling point. After recrystallisation from *o*-dichlorobenzene it had m. p. 266° and sublimed with only slight decomposition. It appears to be isomeric with the monobromo-base, but is not attacked by acetic anhydride even in the presence of sulphuric acid and is characterised by a splendid crimson colour in concentrated sulphuric acid.

A somewhat similar behaviour is shown by 3-*tert.*-butylaniline, which can be smoothly monobrominated but on dibromination yields an oily dibromo-base together with a very small amount of another dibromo-compound, which crystallises from *o*-dichlorobenzene in pale red prisms, m. p. 222—226°. This compound also is not attacked by acetic anhydride and gives a crimson solution in concentrated sulphuric acid.

Experimental

Chlorination, unless otherwise stated, was brought about by heating the compound with excess of sulphuryl chloride, removing the excess, and recrystallising the residue from acetic acid.

2-*Amino*-4-tert.-*butyl*-6-*nitrotoluene*.—Sodium sulphide (25 g.) in water (50 c.c.) was added to a boiling solution of 4-*tert.*-butyl-2 : 6-dinitrotoluene (10 g.) in ethanol (60 c.c.). The resultant solution was poured into water, and the precipitate extracted with boiling dilute hydrochloric

acid to yield a crude hydrochloride, which was used to prepare 2-*acetamido*-4-tert.-*butyl*-6-*nitrotoluene*, which crystallised from ethanol in straw-coloured needles, m. p. 139° (Found: C, 62·3; H, 6·7. $C_{13}H_{18}O_3N_2$ requires C, 62·4; H, 7·2%), and 3-tert.-*butyl*-6-*methyl*-5-*nitro*-N-*toluene*-p-*sulphonylaniline* (II), which crystallised from acetic acid in prisms, m. p. 176° (Found: C, 60·0; H, 6·0. $C_{18}H_{22}O_4N_2S$ requires C, 59·6; H, 6·1%).

Bromination of 3-tert.-*Butyl*-6-*methyl*-5-*nitro*-N-*toluene*-p-*sulphonylaniline*.—Excess of *N*-bromosuccinimide was added to the compound dissolved in pyridine and, after a short time, the mixture was decomposed by dilute hydrochloric acid. The precipitate on crystallisation from acetic acid gave a *monobromo-derivative* as prisms, m. p. 199° (Found: C, 49·1; H, 4·7. $C_{18}H_{21}O_4N_2SBr$ requires C, 49·0; H, 4·8%).

Chlorination of 3-tert.-*Butyl*-6-*methyl*-5-*nitro*-N-*toluene*-p-*sulphonylaniline*.—Boiling for 1 hour with sulphuryl chloride gave the *monochloro-derivative*, which formed prisms, m. p. 193° (Found: C, 55·2; H, 5·2. $C_{18}H_{21}O_4N_2SCl$ requires C, 54·5; H, 5·3%).

2 : 6-*Diamino*-4-tert.-*butyltoluene*.—Stannous chloride (33 g.) in concentrated hydrochloric acid (35 c.c.) was added slowly to a boiling solution of 4-*tert.*-butyl-2 : 6-dinitrotoluene (5 g.) in ethanol (50 c.c.). After ½ hr. the ethanol was distilled off, and the residue made strongly alkaline and extracted with ether. The semisolid residue left after evaporation of the ether was recrystallised from aqueous methanol, to yield the *diamine* in plates, m. p. 98° (Found: C, 73·7; H, 10·2. $C_{11}H_{18}N_2$ requires C, 74·2; H, 10·1%). This gave with acetic anhydride 2 : 6-*diacetamido*-4-tert.-*butyltoluene* (IV), which crystallised from ethanol in needles, m. p. 302—304° (Found: C, 68·6; H, 8·2. $C_{15}H_{22}O_2N_2$ requires C, 68·7; H, 8·4%), and with toluene-*p*-sulphonyl chloride 4-tert.-*butyl*-2 : 6-*ditoluene*-p-*sulphonamidotoluene* (III), which crystallised from acetic acid in prisms, m. p. 212° (Found: C, 62·1; H, 6·4. $C_{25}H_{30}O_4N_2S_2$ requires C, 61·7; H, 6·2%). The latter with excess of *N*-bromosuccinimide in pyridine gave a *monobromo-derivative*, which crystallised from acetic acid in prisms, m. p. 217—220° (Found: C, 52·9; H, 5·3; Br, 14·8. $C_{25}H_{29}O_4N_2S_2Br$ requires C, 53·1; H, 5·1; Br, 14·2%).

2 : 6-Diacetamido-4-*tert.*-butyltoluene gave a *dichloro-derivative*, prisms, m. p. 267° (Found: C, 54·3; H, 6·0. $C_{15}H_{20}O_2N_2Cl_2$ requires C, 54·4; H, 6·0%), which with acetic anhydride and sulphuric acid gave the *tetra-acetyl derivative*, which formed needles, m. p. 216°, from acetic acid (Found: Cl, 17·6. $C_{19}H_{24}O_4N_2Cl_2$ requires Cl, 17·1%).

4-*tert.*-Butyl-2 : 6-ditoluene-*p*-sulphonamidotoluene gave a *dichloro-derivative*, needles, m. p. 220—222° (Found: C, 54·1; H, 5·1. $C_{25}H_{28}O_4N_2S_2Cl_2$ requires C, 54·1; H, 5·1%). This was hydrolysed by solution in cold sulphuric acid to the base, which with acetic anhydride and sulphuric acid gave the tetra-acetyl derivative, m. p. 216° (see above). The mother-liquor from the chlorination gave a *trichloro-derivative*, which formed prisms, m. p. 169—171° (Found: C, 50·5; H, 4·3. $C_{25}H_{27}O_4N_2S_2Cl_3$ requires C, 50·9; H, 4·6%), and contained reactive chlorine. It was readily converted by zinc dust in acetic acid into an impure *monochloro-derivative*, which formed prisms, m. p. 220—222°, from acetic acid (Found: C, 58·4; H, 5·6; Cl, 6·1. $C_{25}H_{29}O_4N_2S_2Cl$ requires C, 57·6; H, 5·6; Cl, 6·8%). This was alternatively prepared by the addition of sulphuryl chloride (1 mol.) to a suspension of 4-*tert.*-butyl-2 : 6-ditoluene-*p*-sulphonamidotoluene in warm chloroform and concentration of the resultant solution.

Nitration of 1 : 4-*Dibromo*-2 : 5-*di*-tert.-*butylbenzene*.—(*a*) The compound (10 g.) was added to a mixture of fuming nitric acid (10 c.c.) and sulphuric acid (40 c.c.) and left for 2 days. The product was filtered off, washed with water and dilute aqueous ammonia, and recrystallised from acetone and then ethanol to yield the *mononitro-derivative* (V) (6 g.) as prisms, m. p. 129° (Found: C, 43·0; H, 4·8; N, 3·7. $C_{14}H_{19}O_2NBr_2$ requires C, 42·7; H, 4·8; N, 3·6%). (*b*) The compound (1 g.) was introduced into fuming nitric acid (4 c.c.) and after a short time the mixture was poured on ice. The above mononitro-compound was obtained in inferior yield together with much material, m. p. 87—90°, easily soluble in cold light petroleum.

Attempted reduction of this nitro-compound by addition of stannous chloride in hydrochloric acid to a boiling ethanolic solution was unsuccessful. Long boiling in ethanol with iron powder or treatment in ethanol with sodium amalgam led to no definite products.

3-*Amino*-4-tert.-*butyl*-5-*nitrobenzoic Acid*.—4-*tert.*-Butyl-3 : 5-dinitrobenzoic acid (18 g.) was dissolved in water (120 c.c.) containing concentrated ammonia solution (18 c.c.), warmed to 50°, and saturated with hydrogen sulphide. The solution was evaporated to half-bulk, then filtered from sulphur, and the filtrate was faintly acidified with acetic acid. The crystalline crop (12 g.) was recrystallised from aqueous ethanol, to give 3-*amino*-4-tert.-*butyl*-5-*nitrobenzoic acid* as prisms, m. p. 230° (slight decomp.) (Found: C, 56·0; H, 5·7. $C_{11}H_{14}O_4N_2$ requires

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C, 55·5; H, 5·9%). With acetic anhydride and sulphuric acid it gave an *acetyl derivative*, which crystallised from acetic acid in needles, m. p. 253—255° (Found: C, 55·6; H, 5·9. $C_{13}H_{14}O_3N_2$ requires C, 55·7; H, 5·7%).

3-*Bromo*-4-tert.-*butyl*-5-*nitrobenzoic Acid*.—The diazonium solution prepared by pouring 3-amino-4-*tert.*-butyl-5-nitrobenzoic acid (5 g.) mixed with sulphuric acid (15 c.c.) and sodium nitrite (1·5 g.) on ice was filtered into a solution of cuprous bromide in hydrobromic acid. The resultant precipitate was dissolved in dilute aqueous sodium hydroxide, reprecipitated by hydrochloric acid, and crystallised from acetic acid. 3-*Bromo*-4-tert.-*butyl*-5-*nitrobenzoic acid* was obtained as almost colourless prisms, m. p. 238—241°, which rapidly became red on exposure to light (Found: C, 43·6; H, 4·0. $C_{11}H_{12}O_4NBr$ requires C, 43·7; H, 4·0%). The m. p. was considerably depressed on admixture with the acid, m. p. 240—242°, obtained by nitration of 3-bromo-4-*tert.*-butylbenzoic acid (cf. below). By treatment with thionyl chloride followed by aniline the acid was converted into 3-*bromo*-4-tert.-*butyl*-5-*nitrobenzanilide*, which formed plates, m. p. 193—194°, from acetic acid (Found: C, 54·9; H, 4·4. $C_{17}H_{17}O_3N_2Br$ requires C, 54·1; H, 4·5%).

4-tert.-*Butyl*-3-*iodo*-5-*nitrobenzoic acid*, obtained by pouring the diazonium solution prepared as for the corresponding bromo-acid into potassium iodide solution, it crystallised from acetic acid in prisms, m. p. 229—232°, which rapidly became red on exposure to light (Found: C, 38·3; H, 3·6. $C_{11}H_{12}O_4NI$ requires C, 37·8; H, 3·4%).

3-*Bromo*-4-tert.-*butylbenzoic Acid*.—(*a*) Silver nitrate (27 g.) in water (90 c.c.) was added to a well-stirred mixture of 4-*tert.*-butylbenzoic acid (27 g.), acetic acid (600 c.c.), concentrated nitric acid (90 c.c.), and bromine (7·8 c.c.). Then stirring was continued for ½ hr., and the mixture heated almost to boiling, filtered hot, and diluted until crystals began to appear. The crop (about 16 g.; m. p. *ca.* 170°) was recrystallised from a small bulk of acetic acid to give 3-*bromo*-4-tert.-*butylbenzoic acid* as needles, m. p. 179° (Found: C, 51·6; H, 5·0%; equiv., 258. $C_{11}H_{13}O_2Br$ requires C, 51·4; H, 5·1%; equiv., 257). (*b*) A mixture of *p-tert.*-butylbenzoic acid (20 g.), bromine (12 c.c.) and iron powder (1·5 g.) was gently warmed for 6 hr. and the product suspended in boiling water (300 c.c.) and treated with excess of aqueous ammonia. Ferric hydroxide was filtered off and the bromo-acid, recovered from the filtrate by precipitation with hydrochloric acid, was purified by recrystallisation from acetic acid.

3-Bromo-4-*tert.*-butylbenzoic acid was dissolved by warming with a slight excess of thionyl chloride, and the product distilled. Almost the whole distilled at 170°/30 mm. and set to a mass of needles, m. p. 60—61°. This material was dissolved in a little dry ether and the solution stirred into ammonia solution (*d* 0·88), brisk reaction occurring with precipitation of the amide, m. p. 123°. This (8 g.), without further purification, was added to a solution of sodium hypobromite prepared from sodium hydroxide (12 g.) and bromine (3 c.c.). A clear solution was first obtained which soon became cloudy (evolution of nitrogen and rise in temperature). The resultant 3-bromo-4-*tert.*-butylaniline was removed in steam [alternatively it may be extracted with hot dilute hydrochloric acid, which on cooling deposits the hydrochloride in needles, m. p. 242° (decomp.)] and acetylated, to give 3-bromo-4-*tert.*-butylacetanilide, which crystallised from ethanol in fine needles, m. p. 144° (Shoesmith and Mackie [6] give m. p. 142—143°). The latter was quite different from 2-bromo-4-*tert.*-butylacetanilide, prepared by the addition of bromine (1 mol.) to *p-tert.*-butylacetanilide (12 g.) suspended in acetic acid (40 c.c.). After recrystallisation from ethanol it formed plates, m. p. 159° (Found: C, 53·7; H, 5·8. Calc. for $C_{12}H_{16}ONBr$: C, 53·3; H, 5·9%) (lit.,[7] m. p. 138·5°, 138°, 158°). The acetyl derivative was hydrolysed in ethanol with concentrated hydrochloric acid, and the resultant base, b. p. 150°/20 mm., reacetylated, giving plates, m. p. 159°, and converted also into the *toluene*-p-*sulphonyl derivative*, which crystallised from acetic acid in needles, m. p. 111° (Found: C, 53·2; H, 5·3. $C_{17}H_{20}O_3NSBr$ requires C, 53·4; H, 5·2%).

Nitration of 3-*Bromo*-4-tert.-*butylbenzoic Acid*.—The powdered acid (5 g.) was added slowly to fuming nitric acid (50 c.c.) cooled in ice, and the mixture poured into ice-cold water. The resultant plastic mass was induced to solidify by rubbing it with acetic acid, and the product (2·7 g.; m. p. *ca.* 150°) was purified by extraction with light petroleum, which left undissolved material (0·5 g.) of m. p. *ca.* 220°, and gave a crop, m. p. 157—168°. Both fractions were purified by recrystallisation from acetic acid and gave respectively needles, m. p. 240—242° (Found: C, 43·2; H, 3·7. $C_{11}H_{12}O_4NBr$ requires C, 43·7; H, 4·0; N, 4·6%), and prisms, m. p. 170—172° (Found: C, 43·9; H, 3·6; N, 4·4%). Both of these *acids* formed sparingly soluble sodium salts, which could be readily recrystallised from boiling dilute sodium hydroxide solution.

The acid, m. p. 170—172°, gave an *anilide*, which crystallised from acetic acid in needles, m. p. 219—221° (Found: C, 54·5; H, 4·4. $C_{17}H_{17}O_3N_2Br$ requires C, 54·1; H, 4·5%). The other acid gave an *anilide*, which crystallised from acetic acid in plates, m. p. 205° (Found: C, 53·9; H, 4·2%).

2 : 5-*Di*-tert.-*butylacetanilide*, prepared from 2 : 5-di-*tert.*-butylaniline, formed plates, m. p. 156°, from ethanol (Found: C, 77·7; H, 9·9. $C_{16}H_{25}ON$ requires C, 77·8; H, 10·1%). It yielded a *monochloro-derivative*, which formed plates, m. p. 185°, from ethanol (Found: C, 68·4; H, 8·4. $C_{16}H_{24}ONCl$ requires C, 68·2; H, 8·6%).

Chlorination of 2 : 5-*Di*-tert.-*butyl*-N-*toluene*-p-*sulphonylaniline*.—(*a*) Chlorine (1 mol.) was passed into a solution of the compound in cold chloroform, and the solution concentrated and diluted with light petroleum. The crop on crystallisation from acetic acid gave the 4-*chloro-derivative* in fine needles, m. p. 170° (Found: C, 64·5; H, 7·2. $C_{21}H_{28}O_2NSCl$ requires C, 64·0; H, 7·1%); it was unchanged after treatment with *N*-bromosuccinimide in pyridine solution. (*b*) Sulphuryl chloride gave 5-tert.-*butyl*-2 : 4-*dichloro*-N-*toluene*-p-*sulphonylaniline* (XI) as needles, m. p. 150° (Found: C, 55·0; H, 5·0; Cl, 19·2. $C_{17}H_{19}O_2NSCl_2$ requires C, 54·8; H, 5·1; Cl, 19·1%), identical with the product of chlorination of 3-*tert.*-butyl-*N*-toluene-*p*-sulphonylaniline. After being kept overnight in concentrated sulphuric acid this compound gave an oily base, which with acetic anhydride gave 5-tert.-*butyl*-2 : 4-*dichloroacetanilide*, m. p. 120—122° (Found: C, 55·3; H, 5·3. $C_{12}H_{15}ONCl_2$ requires C, 55·4; H, 5·8%).

4-Bromo-2 : 5-di-*tert.*-butyl-*N*-toluene-*p*-sulphonylaniline gave 4-*bromo*-5-tert.-*butyl*-2-*chloro*-N-*toluene*-p-*sulphonylaniline* (XII) as needles, m. p. 140° [Found: C, 49·7; H, 4·8. $C_{17}H_{19}O_2NSBrCl$ requires C, 49·0; H, 4·6%; 5·179 mg. gave 4·146 mg. of silver halides (theor., 4·122 mg.)], identical with a sample synthesised in the following way. 4-*tert.*-Butyl-2-nitroaniline was diazotised in concentrated sulphuric acid and converted by the Sandmeyer process into 4-*tert.*-butyl-1-chloro-2-nitrobenzene, which was distilled in steam. The resultant oil, without further purification, was reduced in boiling ethanol by stannous chloride in concentrated hydrochloric acid and the base, after distillation in steam, converted directly into 5-tert.-*butyl*-2-*chloro*-N-*toluene*-p-*sulphonylaniline*, which crystallised from acetic acid in flat needles, m. p. 143° (Found: C, 60·5; H, 5·7. $C_{17}H_{20}O_2NClS$ requires C, 60·4; H, 5·9%). This with *N*-bromosuccinimide in pyridine was converted almost quantitatively into the 4-bromo-derivative, m. p. 140° (cf. above).

2-Bromo-5-*tert.*-butyl-*N*-toluene-*p*-sulphonylaniline gave a *monochloro-derivative* as needles, m. p. 158—160° (Found: C, 48·9; H, 4·5. $C_{17}H_{19}O_2SBrCl$ requires C, 49·0; H, 4·6%).

4-*tert.*-Butyl-3 : 5-dinitrobenzoic acid with quinoline and copper at 200° gave in good yield 2-tert.-*butyl*-1 : 3-*dinitrobenzene*, readily volatile in steam and crystallising from ethanol in plates, m. p. 106° (Found: N, 12·8. $C_{10}H_{12}O_4N_2$ requires N, 12·5%). Similarly, 4-*tert.*-butyl-2 : 5-dinitrobenzoic acid gave 2-tert.-*butyl*-1 : 4-*dinitrobenzene*, also easily volatile in steam and crystallising from ethanol in needles, m. p. 98° (Found: N, 12·6%). A mixture of the two isomerides melted below 80°.

4-tert.-*Butyl*-2 : 6-*dinitroaniline*.—4-*tert.*-Butyl-2-nitroacetanilide (11 g.) was introduced slowly into fuming nitric acid (50 c.c.) cooled in ice, and the resultant solution poured into iced water. The sticky precipitate, recrystallised from ethanol, gave 4-tert.-*butyl*-2 : 6-*dinitro-acetanilide* as yellow needles, m. p. 132° (4·3 g.) (Found: N, 15·3. $C_{12}H_{15}O_5N_3$ requires N, 14·9%). This was hydrolysed in ethanol by aqueous potassium hydroxide to give in poor yield the corresponding base; a considerable amount of alkali-soluble material was produced at the same time. The 4-tert.-*butyl*-2 : 6-*dinitroaniline* was purified by distillation in steam, followed by crystallisation from ethanol, and formed bright yellow, flat needles, m. p. 130° (Found: C, 49·5; H, 5·5; N, 17·1. $C_{10}H_{13}O_4N_3$ requires C, 50·2; H, 5·4; N, 17·6%). The base was unchanged after treatment with toluene-*p*-sulphonyl chloride in pyridine but was readily acetylated by acetic anhydride in presence of sulphuric acid.

Bromination of 2 : 5-*Di*-tert.-*butylaniline*.—The method of Bartlett, Roha, and Stiles [12] gave a black oil, which was dissolved in ethanol and allowed to cool. The small reddish residue was very sparingly soluble in boiling ethanol or acetone but recrystallised from ethyl acetate or *o*-dichlorobenzene in pale red prisms, m. p. 262—266° (Found: C, 59·0; H, 7·1; N, 4·6; Br, 27·7. $C_{14}H_{22}NBr$ requires C, 59·1; H, 7·7; N, 4·9; Br, 28·2%).

Bromination of 3-tert.-*Butylaniline*.—When bromine or *N*-bromosuccinimide (1—3 mols.) was added to the base in pyridine there was always produced in very small amount a compound which was readily isolated owing to its very small solubility. This after recrystallisation

from *o*-dichlorobenzene formed red prisms, m. p. 222—226° (Found: C, 40·1; H, 3·7; N, 4·6; Br, 51·8. $C_{10}H_{13}NBr_2$ requires C, 39·1; H, 4·2; N, 4·6; Br, 52·1%).

1 : 4-*Diamino*-2 : 5-*di*-tert.-*butylbenzene*.—Stannous chloride (49 g.) in hydrochloric acid (60 c.c.) was added to a boiling suspension of 2 : 5-di-*tert.*-butyl-1 : 4-dinitrobenzene (11·4 g.) in ethanol (150 c.c.). The momentarily clear solution soon deposited crystals, which were filtered off and decomposed by aqueous sodium hydroxide, and the product was dried and extracted with boiling benzene. On cooling, the extract deposited the *diamine* as rosettes, m. p. 172—173° (Found: C, 76·0; H, 10·3. $C_{14}H_{24}N_2$ requires C, 76·4; H, 10·9%). On addition of bromine (2 mols.) in acetic acid to a cold solution of the diamine in acetic acid there was obtained 2 : 5-di-*tert.*-butylbenzoquinone, which crystallised from ethanol in yellow needles, m. p. 153° (Found: C, 76·5; H, 8·8. Calc. for $C_{14}H_{20}O_2$: C, 76·4; H, 9·1%). This quinone was unchanged after treatment with sulphur dioxide in boiling 80% ethanol.

By addition of *N*-bromosuccinimide (2 mols.) to the diamine in pyridine there was obtained 2 : 5-*di*-tert.-*butylbenzoquinone dibromodi-imide* which crystallised from ethanol in yellow plates, m. p. 121° (Found: C, 45·4; H, 5·0; Br, 41·7. $C_{14}H_{20}N_2Br_2$ requires C, 44·7; H, 5·3; Br, 42·5%).

The diamine was diazotised either in concentrated sulphuric acid or by Hodgson and Walker's method [14] and the diazonium solution, filtered from much 2 : 5-di-*tert.*-butylbenzoquinone, poured into potassium iodide solution. **1 : 4-*Di*-tert.-*butyl*-2 : 5-*di*-*iodobenzene*** was precipitated and after repeated recrystallisation from ethanol formed needles, m. p. 138° (Found: C, 37·8; H, 4·7; I, 57·2. $C_{14}H_{20}I_2$ requires C, 38·0; H, 4·5; I, 57·5%). The author is indebted to Dr. K. R. Buck for the following observation, " The dipole moment of this di-iodo-compound measured in dilute solution in benzene is, owing to the insensitivity of the method in the range 0—0·6 D, not clearly distinguishable from zero (cf. Kofod, Kumar, and Sutton [4])."

A mixture of the di-iodo-compound (0·75 g.), fuming nitric acid (0·75 c.c.), and sulphuric acid (3 c.c.) was left for 2 days, then filtered (the filtrate on dilution deposited iodine). The sticky product was dissolved in a little acetone and the filtered solution diluted, giving a crop, m. p. 90—95°. This material after two recrystallisations from ethanol gave **1 : 4-*di*-tert.-*butyl*-2-*iodo*-5-*nitrobenzene*** as needles, m. p. 97° (Found: C, 46·4; H, 5·4. $C_{14}H_{20}O_2NI$ requires C, 46·5; H, 5·5%).

The author is indebted to Dr. J. W. Minnis for the microanalyses, and to the Carnegie Trust for the Universities of Scotland for a grant.

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[14] Hodgson and Walker, *J.*, 1935, 530.

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26. *Structural Chemistry of the Alkoxides. Part X.* Primary Alkoxides of Tervalent Iron.*

By D. C. BRADLEY, R. K. MULTANI, and W. WARDLAW.

Ferric alkoxides, $Fe(OR)_3$ where R = Me, Et, Pr^n, Bu^n, Bu^i, $CH_2{\cdot}CMe_3$, $CH_2{\cdot}CHMeEt$, $CH_2{\cdot}CH_2{\cdot}CHMe_2$, and $[CH_2]_4Me$, have been obtained either from ferric chloride, the alcohol, and ammonia, or by alcohol interchange. All except the methoxide volatilise unchanged under reduced pressure. Molecular weights were determined ebullioscopically in benzene and all the compounds, except the *neo*pentyloxide (dimer), were found to be trimeric.

LITTLE is known about ferric alkoxides. Although Grimaux [1] and then Vorlander [2] attempted to prepare ferric ethoxide by treating ferric chloride with sodium ethoxide they did not isolate it pure, and it was not until 1929 that Thiessen and Koerner [3] obtained it by the same method. Meerwein and Bersin [4] reported that ferric ethoxide could be titrated

* Part IX, *J.*, 1957, 2600.

[1] Grimaux, *Bull. Soc. chim.*, 1884, 157.
[2] Vorlander, *Ber.*, 1913, **46**, 181.
[3] Thiessen and Koerner, *Z. anorg. Chem.*, 1929, **180**, 65.
[4] Meerwein and Bersin, *Annalen*, 1929, **476**, 113.

with sodium ethoxide in alcoholic benzene, thymolphthalein being the indicator. Their end-point corresponded to the formation of the double alkoxide $Na[Fe(OEt)_4]$ but this was not isolated. As no other ferric alkoxides had been mentioned it seemed worth while systematically to study their preparation and properties, and in particular to compare ferric alkoxides with aluminium alkoxides.

We now report results on the primary alkoxides mentioned in the summary. The above method for preparing ferric ethoxide was found to be unsuitable because of its low solubility in alcohol, and, although the ethoxide was soluble in benzene, it was difficult to filter off sodium chloride from alcoholic benzene. Ferric chloride in alcoholic solution reacted exothermically on treatment with ammonia, but the ferric ethoxide appeared to be completely coprecipitated with the ammonium chloride. This was due to the formation of an insoluble ammoniate of ferric ethoxide $Fe(OEt)_3,xNH_3$ (where $x = 1$—3), but removal of solvent under reduced pressure led to dissociation of the ammoniate. The ferric ethoxide was then isolated by extraction with benzene, in which it is very soluble. The formation of the ammoniate was demonstrated by exposing the ferric ethoxide, dissolved in either ethyl alcohol or benzene, to ammonia vapour, whereupon a precipitate was formed. This was shown to be a reversible system by pumping off the ammoniacal solvent; ferric ethoxide was regenerated and could be redissolved. A number of ferric primary alkoxides were then prepared by the ammonia method:

$$FeCl_3 + 3ROH + 3NH_3 \longrightarrow Fe(OR)_3 + 3NH_4Cl$$

where R = Me, Et, Pr^n, Bu^n, Bu^i, $CH_2{\cdot}CHMeEt$, $CH_2{\cdot}CH_2{\cdot}CHMe_2$, and $[CH_2]_4Me$.

Several alkoxides were also prepared by alcohol interchange from ferric ethoxide:

$$Fe(OEt)_3 + 3ROH \longrightarrow Fe(OR)_3 + 3EtOH$$

where R = Me, Pr^n, Bu^n, Bu^i, $[CH_2]_4Me$, and $CH_2{\cdot}CMe_3$.

Ferric methoxide was an orange microcrystalline solid soluble in methyl alcohol and in benzene, thus differing from the methoxides of aluminium, titanium, zirconium, hafnium, cerium, and thorium which are insoluble. However, ferric methoxide was involatile and decomposed at 250°/0·05 mm. Ferric ethoxide was a dark brown crystalline compound which melted at 120° and volatilised at 155°/0·1 mm. in a molecular still. It is soluble in benzene and can be recrystallised from ethyl alcohol. Ferric *n*-propoxide was a brown solid which crystallised from benzene and volatilised at 162°/0·1 mm. in the molecular still. Ferric *n*-butoxide and *n*-pentyloxide were both brown, highly viscous liquids which were soluble in benzene and volatilised at 171°/0·1 mm. and 178°/0·1 mm. respectively. The other primary alkoxides (R = Bu^i, $CH_2{\cdot}CMe_3$, $CH_2{\cdot}CHMeEt$, and $CH_2{\cdot}CH_2{\cdot}CHMe_2$) were brown solids which sublimed under reduced pressure. The molecular weights of ferric alkoxides

TABLE 1.

R in $M(OR)_3$	Mol. complexity Fe	Mol. complexity Al	Volatility Fe	Volatility Al
Me	2·9	—	—	—
Et	2·9	4·1	155°/0·1	162°/1·3
Pr^n	3·0	4·0	162°/0·1	205°/1·0
Bu^n	2·9	3·9	171°/0·1	242°/0·7
Bu^i	3·0	—	173°/0·1	—
$Me{\cdot}[CH_2]_4$	3·0	4·0	178°/0·1	255°/1·0
$Me_2CH{\cdot}[CH_2]_3$	3·0	4·0	(decomp.) 200°/0·1	195°/0·1
$MeEtCH{\cdot}CH_2$	3·0	4·1	178°/0·1	200°/0·6
$Me_3C{\cdot}CH_2$	2·0	2·0	159°/0·1	180°/8·0

were determined ebullioscopically in benzene and their molecular complexities are given in Table 1, together with their volatilities (the temperature at which condensate was first observed on the cold-finger of the molecular still). The molecular complexities and b. p.s of the corresponding aluminium alkoxides obtained by Mehrotra [5] are also shown.

[5] Mehrotra, *J. Indian Chem. Soc.*, 1953, **30**, 585; 1954, **31**, 85.

The molecular complexities of the ferric normal alkoxides being considered first, it is noteworthy that they are all trimeric independently of chain length from methyl to *n*-pentyl. Moreover, a moderate degree of branching in the pentyl group does not affect the molecular complexity but the effect of pronounced branching on the β-carbon atom is revealed in the *neo*pentyloxide which is dimeric. It seems reasonable to assume that the complex ferric alkoxides arise through covalency-expansion of the ferric atom which is involved in intermolecular bonding with alkoxide oxygen. In this respect ferric alkoxides behave similarly to those of aluminium, titanium, zirconium, hafnium, cerium, thorium, niobium, and tantalum. Furthermore, in each case the *neo*pentyloxide was characterised by abnormal behaviour due to the steric effect of the *neo*pentyloxide group. The comparison between alkoxides of iron and aluminium is especially interesting because these metals have practically the same covalent radius (1·22 Å and 1·26 Å, respectively [6]) and from the stereochemical viewpoint their alkoxides should have similar properties. However, Table 1 shows that the aluminium alkoxides (mol. complexity 4·0) are more polymerised than the ferric compounds (mol. complexity 3·0) and only the *neo*pentyloxides behave the same. It appears from these data that the intermolecular bonding must be stronger in aluminium alkoxides than in the ferric compounds. The data on volatilities are not strictly comparable because the values quoted for the aluminium compounds are b. p.s of liquids whereas the values for the ferric compounds were obtained under different conditions. Nevertheless, it is clear that in ascending the homologous series from methyl to *n*-pentyl there is a much greater change in volatility in the aluminium compounds than in the ferric compounds.

Experimental

The usual precautions [7] were taken to avoid hydrolysis. Ferric chloride was resublimed in nitrogen at 300° immediately before use (Found: Fe, 34·4; Cl, 65·6. Calc. for Fe_2Cl_6: Fe, 34·4; Cl, 65·6%). Iron was determined gravimetrically as ferric oxide after dissolving the sample in dilute nitric acid. Methoxide and ethoxide determinations were carried out by the chromic acid method [8] with a correction for the reduction of ferric iron by iodide in the back titration.

Preparation of Alkoxides by the Ammonia Method.—The detailed preparation of ferric ethoxide is given as typical. Ferric chloride (15 g.), dissolved in benzene (150 g.) and ethyl alcohol (60 g.), was treated with excess of ammonia. After completion of the exothermic reaction the excess of ammonia and solvents were evaporated off under reduced pressure. The residue was extracted with benzene (150 c.c.), and the ammonium chloride filtered off. The filtrate was evaporated to dryness under reduced pressure and gave a viscous brown residue which dissolved in ethyl alcohol (30 c.c.). Dark brown crystals (4·2 g.) of *ferric ethoxide* were slowly deposited [Found: Fe, 29·3; EtO, 70·7. $Fe(OEt)_3$ requires Fe, 29·3; EtO, 70·7%]. The data concerning the other alkoxides prepared by this method are given in Table 2.

Table 2.

R in $Fe(OR)_3$	Fe_2Cl_6 (g.)	C_6H_6 (g.)	ROH (g.)	$Fe(OR)_3$ (g.)	Fe (%) Found	Fe (%) Calc.
Me	10·45	120	50·0	6·8 *	37·1	37·5
Pr^n	7·8	150	50·0	4·0	23·9	24·0
Bu^n	11·2	200	50·4	4·7	20·2	20·3
Bu^t	8·0	200	50·0	4·0	20·2	20·3
n-C_5H_{11}	8·0	140	40·0	2·9	17·4	17·6
$Me_2CH{\cdot}CH_2{\cdot}CH_2$	12·5	175	50·0	5·6	17·4	17·6
$MeEtCH{\cdot}CH_2$	11·0	200	39·0	4·9	17·5	17·6

* Found: MeO, 62·6. $Fe(OMe)_3$ requires MeO, 62·5%.

[6] Sidgwick, "The Chemical Elements and Their Compounds," Oxford, 1950, Vol. 1, p. xxix.
[7] Bradley, Mehrotra, and Wardlaw, *J.*, 1952, 4204.
[8] Bradley, Halim, and Wardlaw, *J.*, 1950, 3451.

Preparation of Alkoxides by Alcohol Interchange.—The details of the preparation of ferric *n*-propoxide illustrate the method. Ferric ethoxide (5 g.) was dissolved in benzene (80 g.) and *n*-propyl alcohol (35 g.) and the solution was fractionally distilled. The ethyl alcohol liberated in the reaction was removed as the benzene–alcohol azeotrope and the solution was then evaporated to dryness under reduced pressure. *Ferric* n-*propoxide* (6·08 g.) was obtained as a brown solid [Found: Fe, 23·9. $Fe(OPr)_3$ requires Fe, 24·0%]. The details of the other preparations are given in Table 3. The technique used was that described for the *n*-propoxide except that for ferric methoxide the fractionation procedure was omitted and the mixture of methyl and ethyl alcohols was evaporated off under reduced pressure. The product was repeatedly treated with fresh methyl alcohol until interchange was complete.

TABLE 3.

R in $Fe(OR)_3$	C_6H_6 (g.)	$Fe(OEt)_3$ (g.)	ROH (g.)	$Fe(OR)_3$ (g.)	Fe (%) Found	Calc.
Me	—	5·0	(50 + 50 + 50 + 50)	3·8 *	37·3	37·5
Pr^n	100	4·2	75	5·1	24·2	24·0
Bu^n	80	3·0	58·5	4·2	20·2	20·3
Bu^i	100	3·5	45	4·4	20·2	20·3
Am^n	80	4·9	50	8·1	17·8	17·6

* Found: MeO, 62·7. $Fe(OMe)_3$ requires MeO, 62·5%.

Molecular Weights.—Ebullioscopic measurements were carried out in the all-glass apparatus previously described.[9] The results given in Table 4 were obtained by the earlier method [7] involving the use of a calibration constant for the apparatus. When the ferric alkoxides differed considerably from aluminium alkoxides in molecular complexity some molecular weights were also determined by the more accurate "internal calibration" method.[10] These results are given in Table 5.

TABLE 4.

R in $Fe(OR)_3$	Range of *m* (g.)	Wt. of C_6H_6 (g.)	$\Delta T/m$ (°/g.)	*M*	R in $Fe(OR)_3$	Range of *m* (g.)	Wt. of C_6H_6 (g.)	$\Delta T/m$ (°/g.)	*M*
Me	0·0423—0·2834	18·20	0·351	446·0	Bu^i	0·0476—0·3242	17·92	0·199	824·5
Et	0·0481—0·3110	17·80	0·291	569·5	$n\text{-}C_5H_{11}$	0·0599—0·4612	17·81	0·174	951·0
Pr^n	0·0511—0·2944	18·62	0·226	698·5	$Me_3C\cdot CH_2$	0·0349—0·3862	18·00	0·258	634·0
Bu^n	0·0467—0·3146	18·52	0·199	797·0					

TABLE 5.

	Alkoxide		Fluorene		
R in $Fe(OR)_3$	Range of *m* (g.)	$\Delta T/m$ (°/g.)	Range of *m* (g.)	$\Delta T/m$ (°/g.)	*M*
Et	0·0481—0·3110	0·291	0·0031—0·0255	1·002	572
Pr^n	0·0511—0·2944	0·226	0·0046—0·0526	0·954	701
Bu^n	0·0423—0·3060	0·204	0·0216—0·0651	0·985	806

One of us (R. K. M.) thanks the Hans Raj College (Delhi University) for study leave.

BIRKBECK COLLEGE, MALET STREET, LONDON, W.C.1. [*Received, August 23rd,* 1957.]

[9] Bradley, Gaze, and Wardlaw, *J.*, 1955, 3977.
[10] Bradley, Wardlaw, and Whitley, *J.*, 1956, 5.

XUM

27. *The Reactivity of O-Acylglycosyl Halides. Part VI.* Steric Effects of Neighbouring Groups.*

By G. L. Mattok and G. O. Phillips.

Reaction rates at varying temperatures were measured for the S_N1 solvolysis of a series of *O*-acylglycosyl halides, which proceed by way of an open carbonium-ion intermediate. The size and disposition of substituted groups markedly influence the reactivity of the halogen, and this may be accounted for almost entirely by the variation in $\Delta H^{\ddagger}$; $\Delta S^{\ddagger}$ is almost independent of these factors. An interpretation is proposed, by consideration of the conditions operating in the transition state of the reaction. In this way the completely different influence on reactivity at the lactol-carbon atom shown by similar structural changes in the hexose molecule may be explained.

The disposition and size of the substituted groups in a hexose molecule exert an important influence on the reactivity at the lactol-carbon atom.[1] In the previous paper of this series, participation of a 2-acetyl group in the solvolysis of 1 : 2-*trans*-*O*-acetylglycosyl halides was considered. The enhanced rate of solvolysis of these compounds compared with that of the corresponding 1 : 2-*cis*-compounds was accounted for on this basis. However, other factors, probably of steric origin, also influence the reactivity of these compounds, as shown by the marked differences in the reactivity of the two 1 : 2-*trans*-halides, tetra-*O*-acetyl-β-D-glucosyl and α-D-mannosyl halides. In this paper these factors are considered further.

Previously we attempted to rationalise the reactivity of *O*-acetylglycosyl halides on the basis of steric conditions near the halogen atom.[2] Consideration of the steric conditions operating in the transition state of reaction, however, would allow a clearer understanding of the main factors and this is the approach we adopt in this paper. Thus, a distinction must be drawn between the two courses which the solvolyses of *O*-acylglycosyl halides follow, since the steric requirements of forming the transition state from the initial state will be different in each case: in one case there is no participation by the 2-group and an " open-ion " intermediate is formed, and in the second a cyclic-ion intermediate is formed.[3]

The compounds studied in this paper are considered to belong to the former category. Lemieux and Brice [4] recently discussed the reactivity of sugar 1 : 2-*trans*-acetates, which proceed by way of a cyclic-ion intermediate. Here the 3-group exerts the dominant influence on reactivity and the rôle of the 5-group is relatively unimportant. This has been rationalised on the basis of steric inhibition to the formation of the resonance-stabilised, intermediate, 1 : 2-cyclic carbonium ion in the 2 : 3-*cis*-compounds. We shall show, however, that for the " open-ion " type of reaction the 5-group is dominant, a fact which may be understood on consideration of the conditions in the transition state. In this sense, therefore, the investigations are complementary.

Results

Reactions of 1 : 2-trans-*Halides.*—Results for the uncatalysed solvolysis of 3 : 4 : 6-tri-*O*-acetyl-2-*O*-trichloroacetyl-β-D-glucosyl chloride (I) and the 3 : 4 : 6-triacetate 1-chloride (II) were given previously; [2] they are now supplemented with data for the catalysed reactions. The uncatalysed solvolysis was shown to proceed by the S_N1 mechanism.[3] In view of the close relation between this reaction and the solvolysis catalysed by mercuric chloride,[5] the catalysed

* Part V, *J.*, 1957, 268.

[1] Isbell and Frush, *J. Res. Nat. Bur. Stand.*, 1940, **24**, 125; Fletcher and Hudson, *J. Amer. Chem. Soc.*, 1948, **70**, 4052; Lemieux, *Canad. J. Chem.*, 1956, **34**, 1007.
[2] Newth and Phillips, *J.*, 1953, 2904.
[3] Mattok and Phillips, *J.*, 1957, 268.
[4] Lemieux and Brice, *Canad. J. Chem.*, 1956, **34**, 1006.
[5] Mattok and Phillips, *J.*, 1956, 1836.

reaction also probably proceeds by way of the intermediate carbonium ion. As confirmation the reaction order was determined for the methanolysis of 3 : 4 : 6-tri-*O*-acetyl-2-*O*-trichloroacetyl-β-D-glucosyl chloride catalysed by mercuric chloride. As in all other cases investigated, the kinetics are of the first power in both the sugar halide and the mercuric chloride. Table 1 shows the second-order constants. Further solvolysis results, including temperature effects and thermodynamic constants for this reaction and for the solvolysis of the 3 : 4 : 6-tri-O-acetyl-β-D-glucosyl chloride, are given in Tables 2 and 3.

TABLE 1. *Solvolysis of* 3 : 4 : 6-*tri*-O-*acetyl*-2-O-*trichloroacetyl*-β-D-*glucosyl chloride in methanol at* 25°, *catalysed by mercuric chloride.*

RCl (10^3M)	4·9	5·15	5·7	3·85
$HgCl_2$ (10^3M)	5·5	4·1	4·1	5·05
10^4k_2 (l. mole^{-1} sec.$^{-1}$)	5·0	5·12	5·12	5·49

TABLE 2. *Solvolysis of* 3 : 4 : 6-*tri*-O-*acetyl*-2-O-*trichloroacetyl*-β-D-*glucosyl chloride in* 100% *methanol, catalysed by mercuric chloride.*

Temp.	23·5°	25·0°	29·1°	29·6°	32·5°	33·2°
10^4k_2 (l mole^{-1} sec.$^{-1}$)	4·91	5·42	7·52	7·75	9·52	9·75
E (kcal. mole^{-1})			16·6			
$\Delta G^{\ddagger}$ (kcal. mole^{-1}) (at 25°)			22·0			
$\Delta H^{\ddagger}$ (kcal. mole^{-1}) (at 25°)			16·0			
$\Delta S^{\ddagger}$ (e.u.) (at 25°)			−20·1			

TABLE 3. *Solvolysis of* 3 : 4 : 6-*tri*-O-*acetyl*-β-D-*glucosyl chloride in* 100% *methanol catalysed by mercuric chloride.*

Temp.	22·5°	25·4°	31·0°
10^3k_2 (l mole^{-1} sec.$^{-1}$)	7·02	8·61	12·7
E (kcal. mole^{-1})		12·5	
$\Delta G^{\ddagger}$ (kcal. mole^{-1}) (at 25°)		19·0	
$\Delta H^{\ddagger}$ (kcal. mole^{-1}) (at 25°)		11·9	
$\Delta S^{\ddagger}$ (e.u.) (at 25°)		−23·8	

Reactions of 1 : 2-cis-*Halides.*—The methanolysis of several 1 : 2-*cis*-acetylglycosyl halides was investigated, in the absence and presence of mercuric chloride. The halides chosen allowed consideration of (*a*) the effect of the 2-group and, in particular, the function of the oxygen atom, (*b*) the effect of the 6-group, and (*c*) the effect of increasing the size of the substituent groups throughout the glucose molecule. Throughout the rates were calculated by using the initial slope method as described in previous papers, to avoid complications due to subsequent mutarotation.

(a) *Variation of the 2-group.* The effect of temperature on the methanolysis of 2-acetamido-3 : 4 : 6-tri-*O*-acetyl-2-deoxy-α-D-glucosyl chloride (III) is shown in Table 4. For comparison with previous catalysed reactions studied, the rate of solvolysis of 3 : 4 : 6-tri-*O*-acetyl-2-*O*-toluene-*p*-sulphonyl-β-D-glucosyl chloride in methanol catalysed by mercuric chloride was measured, giving $k_2 = 1{\cdot}78 \times 10^{-5}$ l. mole^{-1} sec.$^{-1}$ at 25°.

TABLE 4. *Solvolysis of* 2-*acetamido*-3 : 4 : 6-*tri*-O-*acetyl*-2-*deoxy*-α-D-*glucosyl chloride in* 100% *methanol.*

Temp.	56·8°	30·2°	25·8°
10^4k_1 (sec.$^{-1}$)	14·9	1·79	1·14
E (kcal. mole^{-1})		17·1	

TABLE 5. *Solvolysis of tri*-O-*acetyl*-α-D-*xylosyl chloride in* 100% *methanol in the absence and in the presence of mercuric chloride.*

[$HgCl_2$] = nil.			[$HgCl_2$] = 0·05M.		
Temp.	10^3k_1 (sec.$^{-1}$)	E (kcal. mole^{-1})	Temp.	10^3k_2 (mole^{-1} sec.$^{-1}$)	E (kcal. mole^{-1})
25·5°	5·60		21·6°	3·05	
27·8	6·60		25·0	3·89	
29·5	8·35	17·9	27·4	5·22	15·6
31·3	9·88		29·2	6·04	
32·8	11·3		31·4	7·13	

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(b) ***Variation of the 6-group.*** The results for the catalysed and uncatalysed solvolysis of tri-*O*-acetyl-α-D-xylosyl chloride (IV) in methanol are given in Table 5.

(c) ***Effect of increasing the size of the groups.*** The catalysed solvolysis of tetra-*O*-toluene-*p*-sulphonyl-α-D-glucosyl chloride (V) in methanol is given in Table 6. The free energies and heats and entropies of activation for the 1 : 2-*cis*-halides investigated are shown in Table 7.

TABLE 6.

Temp.	100°	81°	79·5	67·5°	56·5°
10^5k_1 (l. mole^{-1} sec.$^{-1}$)	98·1	25·7	23·6	6·22	2·75
E (kcal. mole^{-1})			20·0		

TABLE 7. *Free energies and heats and entropies of activation of* 1 : 2-cis-*acetylglycosyl halides in* 100% *methanol at* 25°.

Compound	III (uncat.)	IV	V	IV (uncat.)
$\Delta G^{\ddagger}$ (kcal. mole^{-1}) (at 25°)	23·0	20·8	25·7	23·4
$\Delta H^{\ddagger}$ (kcal. mole^{-1}) (at 25°)	16·5	15·0	19·4	17·3
$\Delta S^{\ddagger}$ (e.u.) (at 25°)	−21·8	−19·5	−21·2	−20·5

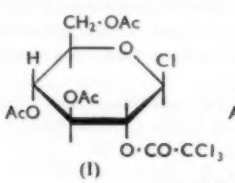
DISCUSSION

The catalysed and uncatalysed solvolysis of the *O*-acetylglucosyl halides are well established as S_N1 type reactions.[5] In each case the intermediate is a carbonium ion and the reactions may be represented:

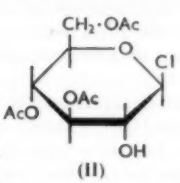
$$R\text{–}Cl \longrightarrow R^+ + Cl^-$$

$$RCl + HgCl_2 \longrightarrow R^+ + HgCl_3^-$$

Thus for compounds where the uncatalysed solvolyses are slow, it is possible to obtain comparable data under catalysed conditions. This applies to sugar halides where an "open-ion" intermediate is formed and to halides where there is participation by the 2-group to give a cyclic-ion intermediate. In the present investigation, the sugar halides studied (I—V) are considered to be of the first type, although in two of the compounds the 2-group is *trans* with respect to the halogen (I and II). The structure of both 1 : 2-*trans*-halides investigated (I and II) makes it highly unlikely that there is participation from the 2-groups. The powerfully electron-attracting trichloromethyl group would drastically reduce the nucleophilic affinity of the carbonyl-oxygen atom in "anchimeric assistance."



(I)



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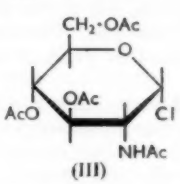

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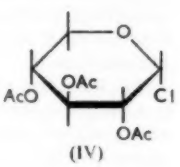
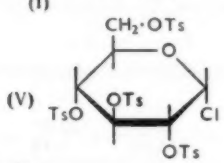
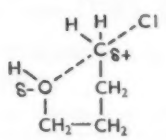


(IV)



(V)

Ts = p-$C_6H_4Me\cdot SO_2$



(VI)

Boschan and Winstein [6] reached a similar conclusion because the rate of acetolysis of *trans*-2-trichloroacetoxy*cyclo*hexyl toluene-*p*-sulphonate is almost three powers of ten slower than that of the corresponding *cis*-compound. The hydroxyl group also shows little tendency for participation,[7] except in rather special circumstances as in the solvolysis of 4-chlorobutan-1-ol. The solvolysis rate for this compound is about 1000 times as rapid

[6] Boschan and Winstein, *J. Amer. Chem. Soc.*, 1956, **78**, 4921.

[7] Winstein and Grunwald, *ibid.*, 1948, **70**, 828; Lemieux and Huber, *Canad. J. Chem.*, 1953, **31**, 1040.

as that of 2-chloroethanol, and it yields tetrahydrofuran.[8] Here anchimeric assistance by the hydroxyl group probably occurs (cf. VI). Normally, however, the presence of the hydroxyl group decreases the rate.[9] Non-participation of the hydroxyl and the trichloromethyl group is further indicated by the nature of the products of solvolysis.[2]

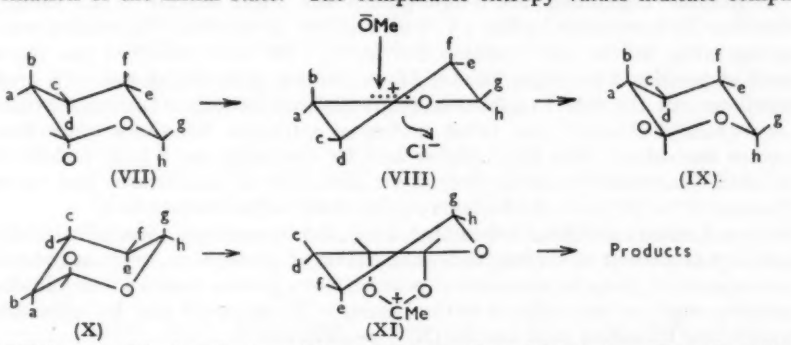
For the 1 : 2-*cis*-halides (III—V), participation by the 2-group can be discounted, and the open-ion intermediate is more likely. Comparative results for solvolysis of these compounds are shown in Table 8. It is clear that for the halides where no cyclic-ion

TABLE 8. *Solvolysis of O-acylglycosyl halides in methanol.*

	$HgCl_2$ present			$HgCl_2$ absent		
Glycosyl chloride	Rel. rate (at 25°)	E (kcal. mole^{-1})	$\Delta S^{\ddagger}$ (e.u.)	Rel. rate (at 25°)	E (kcal. mole^{-1})	$\Delta S^{\ddagger}$ (e.u.)
Tetra-*O*-toluene-*p*-sulphonyl-α-D-glucosyl	1	20·0	−21·2	—	—	—
3 : 4 : 6-Tri-*O*-acetyl-2-*O*-toluene-*p*-sulphonyl-α-D-glucosyl	15·5	—	—	—	—	—
3 : 4 : 6-Tri-*O*-acetyl-2-*O*-trichloroacetyl-β-D-glucosyl	470	16·6	−20·1	—	—	—
Tri-*O*-acetyl-α-D-xylosyl	3380	15·6	−19·5	1	17·9	−20·5
2-Acetamido-3 : 4 : 6-tri-*O*-acetyl-2-deoxy-α-D-glucosyl	—	—	—	2	17·1	−22·0
3 : 4 : 6-Tri-*O*-acetyl-β-D-glucosyl	72,000	12·5	−23·8	2	16	−20·8
Tetra-*O*-acetyl-β-D-glucosyl	—	—	—	3	23	4·70

intermediate is formed the variations in solvolysis rate may be attributed almost entirely to variations in E; $\Delta S^{\ddagger}$ is relatively constant throughout. This may be compared with the dominating influence of $\Delta S^{\ddagger}$ on solvolysis of tetra-*O*-acetyl-β-D-glucosyl chloride, where a cyclic-ion intermediate is formed and the enhanced solvolysis rate depends entirely on the more favourable entropy of activation; the activation energy is slightly less favourable. The variation in reactivity for the halides studies (I—V) is thus consistent with steric factors' being mainly responsible. Previously we have considered steric factors only in their relation to the amount of " bunching " of groups in the vicinity of the halogen.[2]

The dominance of E in controlling reactivity of the 1 : 2-*cis*- and 1 : 2-*trans*-sugar halides studied suggests consideration of the steric conditions operating in the transition state of the reaction. From the results it is unlikely that the compounds differ in the ring conformation of the initial state. The comparable entropy values indicate comparable



(VII) (VIII) (IX)

(X) (XI)

probabilities of achieving the transition state from the initial state. Thus the solvolyses of the *O*-acetylglycosyl halides which proceed by way of an open ion may be represented as in (VII—IX), showing the change in conformation necessary to form the products with inversion. The C1-conformation (VII) is preferred to the 1C conformation (X) because, in the latter, substituents are in the unfavourable axial-positions.

[8] Heine, Miller, Barton, and Greiner, *J. Amer. Chem. Soc.*, 1953, **75**, 4778.
[9] Lemieux, *Adv. Carbohydrate Chem.*, 1954, **9**, 6.

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Entry of the substituting group is predominantly on the side leading to inversion. This could be due to obstruction to the entering group by the departing group on the side leading to retention of configuration, or alternatively to an ion-pair intermediate postulated by Lemieux and Huber.[10] Shielding by substituent groups may also be a contributing factor.

Consideration of the transition state shows that large substituent groups at certain positions would inhibit resonance and achievement of the planar ion. A large 2-group would cause greater interaction between 2- and 3-substituents (a and c), which would account for the relative unreactivity of 3 : 4 : 6-tri-*O*-acetyl-2-*O*-trichloroacetyl-β-D-glycosyl chloride. This effect would probably outweigh the polar influence of the trichloromethyl group which would be weakened by transmission through the saturated carbon atom.

The presence of the larger toluene-*p*-sulphonyl groups would considerably increase the interaction between the 2- and the 3-substituent (a and c) and also between the 4-group and the 6-group (e and g). Similarly, removal of the $-CH_2OAc$ as in (IV) would lead to a release of the latter interaction and a higher reactivity. The reactivity of 2-acetamido-3 : 4 : 6-tri-*O*-acetyl-2-deoxy-α-D-glucosyl compared with that of 3 : 4 : 6-tri-*O*-acetyl-β-D-glucosyl chloride is slightly anomalous if steric factors alone are considered, and suggests that there is a contribution from polar factors. Indeed Lemieux *et al.*[10] found a deactivating influence on progressive replacement of the hydrogen atoms of the acetyl group by chlorine. Some measure of the relative importance of the interaction between 2- and 3-, and between 4- and 6-groups, is given by the relative reactivities of tri-*O*-acetyl-α-D-xylosyl and 3 : 4 : 6-tri-*O*-acetyl-β-D-glucosyl chloride: the former interaction is the more effective but only to a small extent.

The steric effects of the substituent groups described above apply only to the mechanism now under consideration. For another mechanism, it is possible that the same structural changes could lead to different changes in reactivity. This may be demonstrated by reference to reactions at a lactol-carbon atom, which proceed by way of a cyclic-ion intermediate or the open-ion mechanism.

Lemieux and Brice [4] have correlated reactivity and configuration for the reactions of 1 : 2-*trans*-sugar acetates by considering the transition state of the reactions. For these compounds there is participation by the neighbouring 2-acetyl group to form a cyclic-ion intermediate, and here it is the 3-group which exerts the overriding influence on reactivity. For compounds containing 2 : 3-*trans*-groups the sugar acetate is 25 times more reactive than for compounds having a 2 : 3-*cis*-relation, as shown by the relative reactivity of corresponding altrose and mannose derivatives. We have observed this important influence of position 3 for sugar halides whose reaction proceeds by way of a cyclic-ion intermediate. Of the two 1 : 2-*trans*-acetylglycosyl halides, tetra-*O*-acetyl-α-D-mannosyl and -β-D-glucosyl chloride, the latter undergoes solvolysis 380 times faster than the D-mannose derivative. The much higher $\Delta H^{\ddagger}$ for the latter (*ca.* 8 kcal. mole^{-1}) is consistent with deactivation resulting from steric inhibition to achievement and resonance-stabilisation of the ion when the 3-acetoxy-group is *cis* to the 2-substituent.

Further, Lemieux and Brice [4] show that, for 1 : 2-*trans*-acetates, there is little difference in reactivity as a result of varying the configuration of the 4-group, while introduction of the acetoxymethyl group for hydrogen at position 5 of a pentose causes a four-fold decrease in reactivity when in *trans*-relation to the 1-group. These results may be rationalised by reference to the transition state scheme (X) ⟶ (XI), etc.

These results may be compared with the changes in reactivity accompanying similar configurational changes in reactions where no cyclic-ion intermediate is formed. For solvolysis of 1 : 2-*cis*-acetylglycosyl bromides, changing the configuration of the 4-group (glucose–galactose) produces a 4·5-fold change in rate, and introduction of a 5-acetoxymethyl group (glucose–xylose) produces a 50-fold decrease in the reactivity of the halogen.[2] For 1 : 2-*cis*-acetylglycosyl chlorides introduction of the acetoxymethyl group results in a

[10] Lemieux and Huber, *Canad. J. Chem.*, 1955, **33**, 128.

40-fold decrease. The differences arise directly from the difference in the transition state. Reactivity should therefore be related to a particular mechanism.

Experimental

Methanol and acetone were purified as described in earlier papers. The compositions of the solvent mixtures are given according to the convention used throughout this series.

Tri-*O*-acetyl-α-D-xylosyl chloride was prepared by boiling xylose and acetyl chloride in the presence of a trace of zinc chloride; the m. p. was 105° and $[\alpha]_D$ 171° (*c* 2 in $CHCl_3$).

3 : 4 : 6-Triacetyl-2-*O*-trichloroacetyl-β-D-glucosyl chloride was prepared by treating penta-*O*-acetyl-β-D-glucose with phosphorus pentachloride and had m. p. 139° and $[\alpha]_D$ +9° (*c* 2·1 in $CHCl_3$).

3 : 4 : 6-Triacetyl-β-D-glucosyl chloride was prepared by deacetylation of the preceding compound with dry ethereal ammonia; the m. p. was 154—155° and $[\alpha]_D$ +45° (*c* 1·8 in $CHCl_3$).

Tetra-*O*-toluene-*p*-sulphonyl-α-D-glucosyl chloride was prepared by treating a solution of toluene-*p*-sulphonyl chloride in chloroform with glucose in pyridine. The m. p. was 81° and $[\alpha]_D$ 61° (*c* 2 in acetone).

3 : 4 : 6-Tri-*O*-acetyl-2-*O*-toluene-*p*-sulphonyl-α-D-glucosyl chloride was prepared by treating a suspension of tri-*O*-acetyl-β-D-glucosyl chloride in chloroform with toluene-*p*-sulphonyl chloride in pyridine–chloroform. The m. p. was 121° and $[\alpha]_D$ 149° (*c* 1 in acetone).

2-Acetamido-3 : 4 : 6-tri-*O*-acetyl-2-deoxy-α-D-glucosyl chloride, prepared as described by Baker *et al.*,[11] had m. p. 126°.

Rate measurements were carried out in a polarimeter tube (2·2 dm.) kept at constant temperature. For α-D-glucose tetratoluenesulphonate 1-chloride the sealed-ampoule technique, described in Part IV,[12] was used.

The rate constants were calculated from the initial rates of the reaction.

Tables 9—12 show typical runs, only a part of the experimental observations being given. In general the calculated values of the activation energy are accurate to ±0·5 kcal. mole^{-1}.

Table 9. *Solvolysis of tri-*O*-acetyl-α-D-xylosyl chloride in* 100% *methanol at* 29·5°. [RCl] = 0·05M.

Time (min.)	3	7	9	11	15	19	25	31	35	45	55	∞
α	5·25°	5·15°	5·03°	5·97°	4·86°	4·74°	4·55°	4·39°	4·28°	4·01°	3·75°	−1·20°

$(d\alpha/dt)_{t=0}$ = 3·2 × 10^{-2} degree min.$^{-1}$. k = 8·35 × 10^{-5} sec.$^{-1}$.

Table 10. *Solvolysis of 2-acetamido-*3 : 4 : 6*-tri-*O*-acetyl-2-deoxy-α-D-glucosyl chloride in* 100% *methanol at* 25·8°. [RCl] = 0·19M.

Time (min.)	4	15	22	29	36	50	68	82	97	117	151	∞
α	1·89°	1·76°	1·69°	1·61°	1·54°	1·41°	1·24°	1·13°	1·02°	0·90°	0·72°	0·05°

$(d\alpha/dt)_{t=0}$ = 1105 × 10^{-2} degree min.$^{-1}$. k_1 = 1·14 × 10^{-4} sec.$^{-1}$.

Table 11. *Solvolysis* 3 : 4 : 6*-tri-*O*-acetyl-2-*O*-trichloroacetyl-β-D-glucosyl chloride in* 100% *methanol at* 29·6°, *in presence of mercuric chloride.* [RCl] = 0·05M. [$HgCl_2$] = 0·049M.

Time (min.)	5	17	30	40	50	60	70	80	90	100	150	240	∞
α	0·53°	0·67°	0·83°	0·93°	1·02°	1·13°	1·23°	1·32°	1·41°	1·51°	1·96°	2·66°	5·24°

$(d\alpha/dt)_{t=0}$ = 1·1 × 10^{-2} degree min.$^{-1}$. k_2 = 7·75 × 10^{-4} l. mole^{-1} sec.$^{-1}$.

Table 12. *Solvolysis of* 3 : 4 : 6*-triacetyl-*2*-*O*-toluene-*p*-sulphonyl-α-D-glucosyl chloride in* 100% *methanol at* 25°, *in presence of mercuric chloride.* [RCl] = 0·018M. [$HgCl_2$] = 0·018M.

Time (days)	0	7	15	19	22	24	26	29	31	37	∞
α	2·80°	2·45°	2·04°	1·88°	1·65°	1·50°	1·33°	1·08°	0·94°	0·60°	−0·05°

$(d\alpha/dt)_{t=0}$ = 4·44 × 10^{-5} degree min.$^{-1}$. k_2 = 1·78 × 10^{-5} l. mole^{-1} sec.$^{-1}$.

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University College, Cathays Park, Cardiff. [*Received, June 3rd,* 1957.]

[11] Baker, Joseph, Shand, and Williams, *J. Org. Chem.*, 1954, **19**, 1786.
[12] Mattok and Phillips, *J.*, 1956, 1836.

28. *Amine Compounds of the Transition Metals. Part III.* The Reaction of Some Transition-metal Chlorides with Anhydrous Ethylenediamine and Propylenediamine.*

By G. W. A. Fowles and W. R. McGregor.

The reaction of anhydrous ethylenediamine and propylenediamine with transition-metal chlorides has been studied. The more ionic chlorides, vanadium(III) chloride and chromium(III) chloride, are strongly solvated and form $[V\,en_3]Cl_3$, $[V\,pn_3]Cl_3$, and $[Cr\,en_3]Cl_3$ respectively, whereas the covalent titanium(IV), vanadium(IV), and molybdenum(V) chlorides are solvolysed by anhydrous ethylenediamine. Iron(III) chloride is first reduced to the iron(II) state and subsequently forms the "outer-orbital" complex $[Fe\,en_3]Cl_2$. The structure of the reaction products is discussed.

Whereas the ionic halides of metals of Groups Ia, IIa, and IIIa react with ammonia to form simple ammoniates,[1] the ionic halides of the lower-valency states of the transition elements form the cobaltammine type of compound and the more covalent halides of these metals undergo ammonolysis with the formation of ammonobasic halides. While examining the analogous reactions of metal halides with amines, we have examined the reactions of transition-metal chlorides of both ionic and covalent type with anhydrous ethylenediamine and propylenediamine. These amines are interesting in that they can form especially stable chelate compounds with the transition metals.

Experimental

Materials.—Ethylenediamine (en) and propylenediamine (pn) were purified as described previously.[2] Vanadium(III) chloride was made by the thermal decomposition of vanadium(IV) chloride in an atmosphere of carbon dioxide.[3] Iron(III) chloride was prepared by direct chlorination of iron powder, and sublimed; reduction with hydrogen at 300° gave iron(II) chloride. Titanium(IV) chloride (from Messrs. British Drug Houses Ltd.) was refluxed with sodium amalgam and finally vacuum-distilled into sealed tubes. Anhydrous chromium(III) chloride was made by the action of carbonyl chloride on the heated hexahydrate.[4]

Analysis.—Chlorine, nitrogen, and vanadium were determined as previously described.[1] Iron and chromium were estimated by titration of their reduced solutions with potassium dichromate, and titanium by precipitation of the hydroxide followed by ignition to the oxide.

Reactions.—All reactions were carried out with anhydrous materials under rigorously anhydrous conditions, in the usual type of closed vacuum system.[1]

Reaction of vanadium(III) chloride with ethylenediamine and propylenediamine. Vanadium(III) chloride and excess of ethylenediamine were sealed in an ampoule; considerable heat was generated when reaction occurred, and after prolonged shaking a deep red-brown solution remained. On opening the ampoules and pumping away excess of amine (20 hr. at 100°) a homogeneous red-brown *solid* remained (Found: V, 14·9; Cl, 29·1; en, 54·1. $VCl_3,3en$ requires V, 15·1; Cl, 31·5; en, 53·4%). Because of the very viscous solution formed by the vanadium(III) chloride in ethylenediamine, the last traces of amine could only be removed by prolonged pumping; samples pumped for a shorter time contained more ethylenediamine.

The reaction of vanadium(III) chloride with propylenediamine gave a similar *product*; the analyses again show the high amine content which is found if the product is pumped for only a short time ($VCl_3,3pn$ requires V, 13·4; Cl, 28·0; pn, 58·6%).

The slightly low V : Cl ratio is attributed to a little thermal decomposition of vanadium(III) chloride when sealing off the storage tubes; and analysis of the chloride which had been thus sealed off gave a V : Cl ratio of 1 : 2·92.

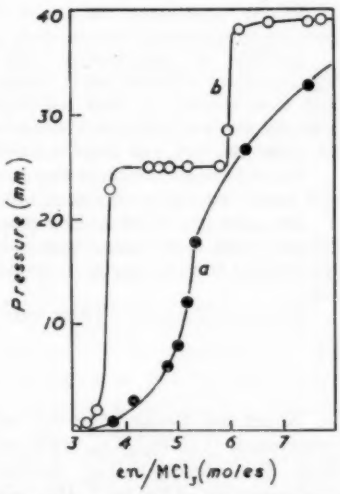
* Part II, Fowles and Pleass, *J.*, 1957, 2078.

[1] Fowles and Pleass, *J.*, 1957, 1674.
[2] Fowles, McGregor, and Symons, *J.*, 1957, 3329.
[3] Young and Smith, *Inorg. Synth.*, 1953, **4**, 128.
[4] Heisig, Fawkes, and Hedin, *Inorg. Synth.*, 1946, **2**, 193.

Time of pumping at 100°	V (%)	Cl (%)	pn (%)	Ratio V : Cl : pn
5 hr.	12·1	24·4	63·1	1 : 2·88 : 3·58
10 hr.	13·3	26·4	59·0	1 : 2·87 : 3·08
24 hr.	13·1	26·7	58·7	1 : 2·92 : 2·91

The analyses of these products indicate that vanadium(III) chloride reacts with anhydrous ethylenediamine and propylenediamine to give VCl_3,3en and VCl_3,3pn respectively, both of which are stable *in vacuo* up to 100°. While the difficulty of removing the last traces of amine could be accounted for by the viscous nature of the solutions formed by the compounds in the amine, it seemed possible that definite amounts of amine might be attached to the compounds in an " ammoniate " manner. A tensimetric investigation (Figure, *a*) of the vanadium(III) chloride–ethylenediamine system at 45° in a modified form of the Burg tensimeter [5] showed conclusively that only VCl_3,3en was formed.

Reaction of chromium(III) *chloride with ethylenediamine.* Simple condensations of excess of ethylenediamine on a known weight of chromium(III) chloride in a weighed jointed tube, complete with stopcock, followed by removal of the excess of amine by prolonged pumping, showed that the chloride took up three molecules of ethylenediamine (Found: $CrCl_3$: en = 1 : 3·18, and 1 : 3·14). The violet chromium(III) chloride reacted with the ethylenediamine as it melted with the liberation of heat and the formation of a deep red solution. A yellow solid began to separate and after several hours a clear colourless supernatant liquid remained.



Tensimetric studies of the ethylenediamine–vanadium trichloride system ● *and the ethylenediamine–chromium trichloride system* ○ *at* 45°.

Ampoules of the reactants were made up, shaken, and opened, and the yellow solid washed with pure ethylenediamine. Evaporation of the filtrate left no residue, showing that no ethylenediamine hydrochloride was formed in the reaction. After overnight pumping at room temperature, the yellow *solid* was analysed (Found: Cr, 15·1; Cl, 29·7; en, 55·2%; Cr : Cl : en, 1·0 : 2·88 : 3·16; $CrCl_3$,3en requires Cr, 15·4; Cl, 31·4; en, 53·2%). Its magnetic moment was 3·83 B.M., showing that chromium is still tervalent.

We conclude that chromium(III) chloride reacts with anhydrous ethylenediamine to give $CrCl_3$,3en.

Since the product is insoluble in ethylenediamine, there should be no difficulty in pumping off the amine, so that the high amine content of the product seems a definite indication of additional compound formation. This was confirmed by a tensimetric study at 45° (Figure, *b*) and 50°, which showed that $CrCl_3$,3en takes up three additional molecules of ethylenediamine. From the dissociation pressures measured at 45° and 50°, ΔH for the equilibrium $CrCl_3$,6en $\rightleftharpoons$ $CrCl_3$,3en + 3en is 18·1 kcal./mole.

Reaction of iron(III) *chloride with ethylenediamine and propylenediamine.* Ethylenediamine reacted immediately with iron(III) chloride (in an ampoule) giving white fumes. After being shaken for several hours, a red-brown solution and an off-white solid remained; these were washed with fresh ethylenediamine until all traces of the red-brown colour of the associated solution had been removed. The red liquid contained almost no iron, but considerable amounts of chloride ion; evaporation of ethylenediamine from this solution left a highly viscous red liquid, which gave some yellowish-white sublimate when heated to 160° *in vacuo*.

The white solid remaining after the initial filtration was pumped for several hours at 45° (Found: Fe, 17·3; Cl, 21·3; en, 61·4%; Fe : Cl : en, 1 : 1·94 : 3·31. $FeCl_2$,3en requires Fe, 18·2; Cl, 23·1; en, 58·7%). Its magnetic moment was 5·45 B.M.

The analysis and colour of the solid suggest that iron(III) chloride has been reduced to give an iron(II) compound, although the magnetic moment is considerably higher than a simple spin-only formula would predict (4·9 B.M.). As it seemed possible that this high value might arise from traces of iron in the iron(III) chloride, this was purified further by sublimation and

[5] Sanderson, " Vacuum Manipulation of Volatile Compounds," Wiley, New York, 1948, p. 79.

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reduced to iron(II) chloride; this reacted with ethylenediamine to give a colourless solution and a white solid (Found: Fe, 18·2; Cl, 23·0; en, 58·8%) which had a magnetic moment of 5·45 B.M. A direct titration of the white product of the iron(III) chloride–ethylenediamine reaction confirmed the bivalency of iron.

We may therefore conclude that iron(III) chloride is reduced by anhydrous ethylenediamine to give $FeCl_2$,3en. The red solution which is formed contains ethylenediamine hydrochloride, but no iron, and the red colour is evidently associated with the oxidation products of the amine.

Iron(III) chloride reacted more slowly, but otherwise similarly, with anhydrous propylenediamine.

Reaction of titanium(IV) *chloride with ethylenediamine.* The initial reaction gave an orange-red solid, which gradually became paler; an almost colourless solid and a clear supernatant liquid finally remained. On being washed with fresh ethylenediamine, followed by pumping, a colourless diamagnetic solid was obtained which had an analysis corresponding to $TiCl_{2\cdot02}N_{3\cdot91}$ (Found: Ti, 13·6; Cl, 20·4%). The filtrate contained large amounts of ethylenediamine hydrochloride.

In one experiment, the use of slightly moist ethylenediamine gave a multicoloured initial product which finally became dirty grey.

Reaction of vanadium(IV) *chloride and molybdenum*(V) *chloride with ethylenediamine.* Vanadium(IV) chloride reacts vigorously with ethylenediamine, initially forming white fumes, and subsequently a deep red-brown solution. Evaporation of ethylenediamine from the solution was very difficult because of its viscosity, and even after pumping for many hours at 70—100° the VCl_4 : en ratio was still 1 : 4·6.

Molybdenum(V) chloride also gave white fumes in its initial reaction with ethylenediamine, and finally formed a very dark brown solution with a little undissolved brown solid.

The products of these two reactions were evidently mixtures of ethylenediamine hydrochloride with some amino-basic chloride; but since these could not be separated (as could the product from titanium) by washing with ethylenediamine, the reactions were not studied in detail.

Magnetic Moments.—These were determined at room temperature on a Gouy balance.

Discussion

Meyer and Backa [6] showed that vanadium(III) chloride forms a cobaltammine type of compound, $[V(NH_3)_6]Cl_3$, with ammonia. This is much less stable to air and moisture than the corresponding chromium compound formed from liquid ammonia and chromium(III) chloride; [7] this may be readily understood since the tervalent vanadium atom still has a vacant 3*d* orbital and should accordingly form labile octahedral complexes.[8]

We might expect both vanadium(III) chloride and chromium(III) chloride to form chelate compounds with diamines, in which both amino-groups co-ordinate with the metal. We expect the vanadium(III) compounds to be labile, so that they would be isolated only under rigorously anhydrous conditions. The reaction of vanadium(III) chloride with both anhydrous ethylenediamine and propylenediamine does give $[V\ en_3]Cl_3$ and $[V\ pn_3]Cl_3$ respectively, and although free diamine can only be removed from the compounds with difficulty, tensimetric studies prove that trisethylenediaminevanadium(III) chloride does not form a true compound with additional ethylenediamine.

We should expect chromium(III) chloride to form an inert compound with ethylenediamine: hydrated trisethylenediaminechromium(III) chloride is formed even from aqueous solutions of ethylenediamine.[9] The greater stability of this compound than of a hydrated chromium(III) ion may be attributed to the chelation associated with the ethylenediamine molecule. Pollinson and Bailar [7] and Linhard and Weigel [10] noted that a yellow compound is formed from anhydrous ethylenediamine and chromium(III) chloride,

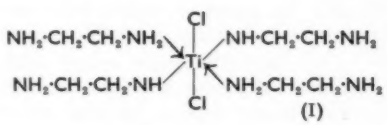
[6] Meyer and Backa, *Z. anorg. Chem.*, 1924, **135**, 177.
[7] Pollinson and Bailar, *J. Amer. Chem. Soc.*, 1943, **65**, 250.
[8] Taube, *Chem. Rev.*, 1952, **50**, 69.
[9] Balthis and Bailar, *J. Amer. Chem. Soc.*, 1936, **58**, 1474.
[10] Linhard and Weigel, *Z. anorg. Chem.*, 1953, **271**, 115.

but both pairs of authors dissolved this substance in water and precipitated the hydrated trisethylenediaminechromium(III) chloride. Our results show that the non-hydrated complex can be readily obtained under anhydrous conditions, but that it may take up three further molecules of ethylenediamine. These three extra ethylenediamine molecules are held quite weakly ($\Delta H = 18{\cdot}1$ kcal./mole) so that the substance $CrCl_3$,6en is probably trisethylenediaminechromium(III) chloride with the three other ethylenediamine molecules bonded by ion–dipole forces, *i.e.*, [Cr en_3]Cl_3,3en. Alternatively, the substance $CrCl_3$,6en may have a structure analogous to that of $[Cr(NH_3)_6]Cl_3$, with one amino-group of each ethylenediamine molecule bonded directly to the chromium atom; with the removal of a diamine molecule, the vacant co-ordination position on the chromium atom could be taken up by the other amino-group of a co-ordinated ethylenediamine molecule. The tensimetric investigation favours the first interpretation, since it does not indicate any intermediate steps in the process

$$CrCl_3,6en \longrightarrow CrCl_3,3en$$

The magnetic moment of 3·83 B.M. confirms the tervalent nature of chromium in the complex, although it cannot distinguish between the alternative orbitals which might be used for bonding—" inner," $3d^24s4p^3$, or " outer," $4s4p^34d^2$. Since the complex is inert, however, neither of the $3d$ orbitals can be vacant, so that the complex must be an inner-orbital one, with the chromium atom using its $3d^24s4p^3$ orbitals for bonding with the nitrogen atoms of the ethylenediamine molecules.

Investigations of the reaction of titanium(IV) chloride with ammonia,[11] and with methylamine and dimethylamine,[12] show that solvolysis occurs with the formation of ammono-basic and amino-basic titanium(IV) chlorides respectively. We should, therefore, expect titanium(IV) chloride to form some amino-basic chloride when it reacts with ethylenediamine, and an insoluble colourless substance $TiCl_2en_{3\cdot9}$ is indeed formed in the reaction; it may be easily separated from the ethylenediamine hydrochloride which is soluble in ethylenediamine. The diamagnetism of the product proves that titanium has not been reduced, while the analysis shows that two chlorine atoms have been replaced by ethylenediamine residues; it seems reasonable to assign the formula $TiCl_2(NH{\cdot}CH_2CH_2{\cdot}NH_2)_2$,2en to the substance. This substance should have an octahedral configuration, with two positions taken up by chelation of the already bound $NH{\cdot}CH_2{\cdot}CH_2{\cdot}NH_2$ unit through the amino-group, and the two remaining ethylenediamine molecules very weakly held. As with the chromium-(III) complex, it is possible that the ethylenediamine molecules are only unidentate, with the compound having the structure (I).



(I form)

(I)

Since vanadium(IV) chloride [1] and molybdenum(V) chloride [13] undergo solvolysis when they react with methylamine and dimethylamine, it is reasonable to attribute the formation of white fumes in their reaction with ethylenediamine to a similar cause, although separation and identification of the products was not possible.

Iron(III) chloride is reported to form an unstable hexammine with ammonia,[14] but with anhydrous ethylenediamine and propylenediamine any iron(III) compound which might form initially undergoes a subsequent reduction and the formation of $FeCl_2$,3en. This is evidently the same compound as that reported by Breuil [15] as the product of the iron(II) chloride–ethylenediamine reaction. $FeCl_2$,3en is best considered as [Fe en_3]Cl_2, and the

[11] Fowles and Pollard, *J.*, 1953, 2588.
[12] Antler and Laubengayer, *J. Amer. Chem. Soc.*, 1955, **77**, 5250.
[13] Fowles and Sandy, unpublished observations.
[14] Newton-Friend, " Text-book of Inorganic Chemistry," Griffin & Co., Ltd., London, 1928, Vol. X, p. 127.
[15] Breuil, *Compt. rend.*, 1933, **196**, 2009.

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magnetic moment of 5·45 B.M. shows that the complex is an " outer-orbital " one with the bivalent iron atom using $4s4p^34d^2$ orbitals for the bonding. The magnetic moment is appreciably greater than the " spin-only " formula would predict for four unpaired electrons (4·9 B.M.), but this is commonly found for outer-orbital iron(II) complexes, Klemm *et al.*[16] reporting a value of 5·3 B.M. for the analogous hexammine, $[Fe(NH_3)_6]Cl_2$, and may be attributed to incomplete quenching of the orbital contribution.

The mechanism of the reduction of iron(III) to iron(II) by the amine is not clear (cf. Part I for brief discussion of the reduction of halides by amines), and a discussion of the process is postponed.

We thank the Esso Petroleum Company for a maintenance grant (to W. R. M.).

THE UNIVERSITY, SOUTHAMPTON. [*Received, July 23rd,* 1957.]

[16] Klemm, Jacobi, and Tilk, *Z. anorg. Chem.*, 1931, **201**, 1.

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29. *Photochemical Transformations. Part II.*[1] *The Constitution of Lumisantonin.*

By D. H. R. BARTON, P. DE MAYO, and MOHAMMED SHAFIQ.

Irradiation of santonin in ethanolic solution affords an isomer, lumisantonin, which has been shown to have the constitution (III). Lumisantonin affords photosantonic acid on irradiation in cold aqueous acetic acid. It is rearranged thermally by hot aqueous acetic acid, to 10-hydroxy-3-oxoguai-4-en-6 : 12-olide (II).

IN Part I of this series[1] the light-induced conversion of santonin (I) into 10-hydroxy-3-oxoguai-4-en-6 : 12-olide (*iso*photosantonic lactone) (II) in aqueous acetic acid was reported. In further experiments on the photochemistry of santonin, directed towards the elucidation of the structure of " photosantonin,"[2] we have discovered a new light-produced isomer. This compound has also been obtained by Professor Büchi (M.I.T.), Professor Jeger (E.T.H., Zürich), and by Professor Cocker (Trinity College, Dublin), whom we thank for their kind personal communications to this effect; they have suggested that it be called lumisantonin, and we are happy to agree. The present paper describes our own work on this compound. It affords the lactone (II) when refluxed with aqueous acetic acid *in the dark* and is an important intermediate in the light-induced reactions of santonin. A preliminary communication proposing the constitution (III) has already appeared.[3]

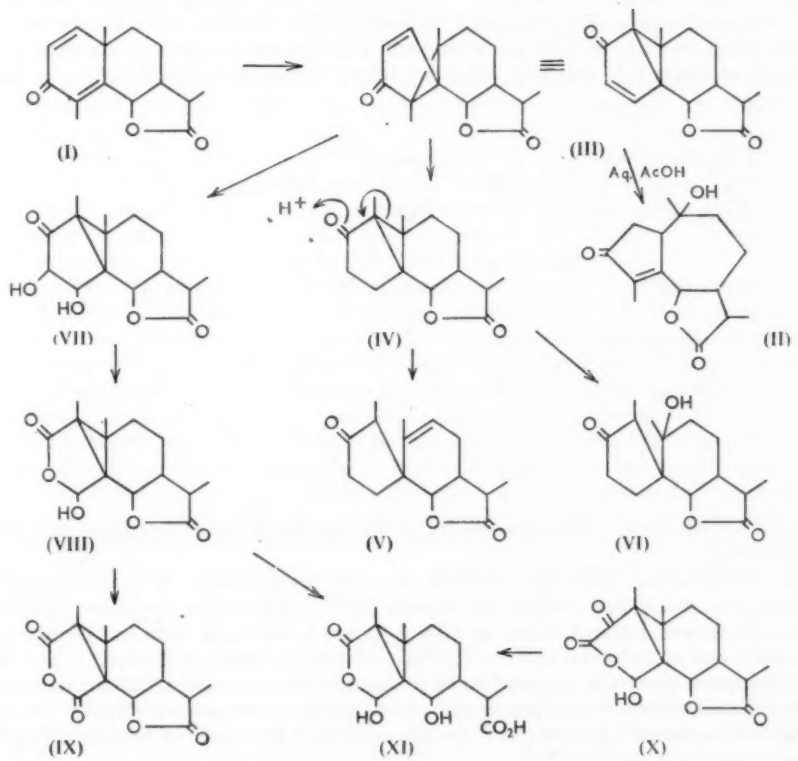
Lumisantonin, obtained along with photosantonin by irradiation of santonin in ethanol solution, is assigned this constitution[3] on the basis of the following evidence. Its infrared spectrum showed bands in Nujol at 1765 (γ-lactone) and 1703 and 1663 cm.$^{-1}$ (αβ-unsaturated *cyclo*pentenone) and in CCl_4 at 1785 (γ-lactone) and 1703 and 1670 cm.$^{-1}$ (αβ-unsaturated *cyclo*pentenone). Its ultraviolet absorption spectrum showed a broad band at 239 mμ (ε 5800) indicative of an αβ-unsaturated ketone. It contained three *C*-Me groups as determined both chemically and by quantitative infrared measurements.

Lumisantonin was readily hydrogenated to a dihydro-derivative (IV) which showed infrared bands at 1770 (γ-lactone) and 1703 cm.$^{-1}$. The identical ketone frequencies in (III) and (IV) are not unexpected, since there is the same relation between the carbonyl frequencies of umbellulone and β-dihydroumbellulone[4] where a comparable structural

[1] Part I, Barton, de Mayo, and Shafiq, *J.*, 1957, 929.
[2] See Simonsen and Barton, " The Terpenes," Cambridge Univ. Press, 1952, Vol. III, p. 292.
[3] Barton, de Mayo, and Shafiq, *Proc. Chem. Soc.*, 1957, 205.
[4] Eastman, *J. Amer. Chem. Soc.*, 1954, **76**, 4115.

change is postulated. The frequency at 1703 cm.$^{-1}$ is, therefore, indicative of a *bicyclo*-[3 : 1]hexan-2-one system. Dihydrolumisantonin gave no colour with tetranitromethane and was stable to ozone, but it showed an ultraviolet absorption maximum at 214 mμ (ε 4600) characteristic [4] of conjugated ketone and *cyclo*propane groups.

When dihydrolumisantonin was refluxed with aqueous acetic acid it furnished an isomer (V) and the corresponding tertiary alcohol (VI). The isomer (V) had three CMe groups and showed infrared bands at 1765 (γ-lactone) and 1735 cm.$^{-1}$ (normal *cyclo*pentanone). It gave a colour with tetranitromethane and showed only an isolated ethylenic linkage in its ultraviolet absorption spectrum. The production of an additional ethylenic linkage under such mild conditions, when coupled with the spectroscopic data, constitutes a proof of the presence of a conjugated ketone group and *cyclo*propane ring in lumisantonin. The constitution (VI) follows from its genesis, the failure to show absorption in the far ultraviolet region, and infrared bands at 3430 (hydroxyl), 1750 (γ-lactone), and 1726 cm.$^{-1}$ (*cyclo*pentanone).

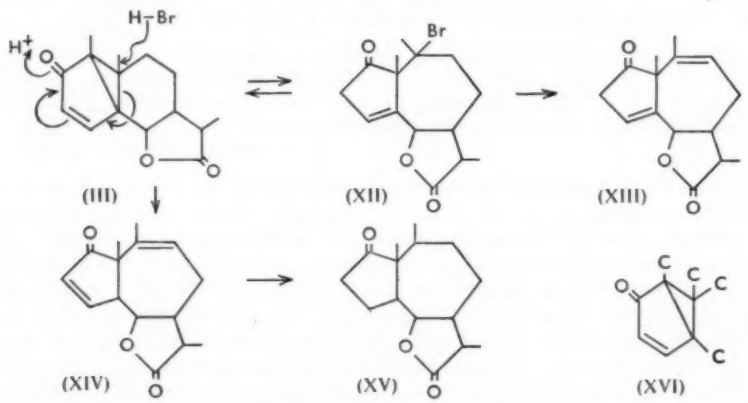


Treatment of lumisantonin (III) with osmium tetroxide furnished a crystalline glycol VII). This gave infrared bands at 3360 (hydroxyl), 1770 (γ-lactone), and 1726 cm.$^{-1}$ (*cyclo*pentanone), had the same ultraviolet absorption as dihydrolumisantonin (IV), and consumed two mols. of periodic acid to afford a C_{14} aldehydo-acid. This acid is regarded as existing in the lactol form (VIII) since it exhibited no ultraviolet or infrared aldehyde absorption. It gave a positive Fehling's test (lumisantonin and its dihydro-derivative

did not, under the same conditions) and consumed one atom of oxygen on titration with chromic acid. The product of oxidation was characterised as an anhydride (IX) by its infrared spectrum which showed bands at 1830 (anhydride) and 1770 cm.$^{-1}$ (superimposed anhydride and γ-lactone bands). The position of the anhydride band at 1830 cm.$^{-1}$ is what might be expected [5] for a succinic anhydride attached to a *cyclo*propane ring.

This evidence conclusively proves the presence of the grouping (CO·CH:CH) in lumisantonin. Ozonolysis studies confirm this. Treatment of lumisantonin with ozone gave formic acid (0·4 mol.) and a small amount of crystalline compound formulated as (X) (or equivalent open formula). This showed infrared bands at 3440 (hydroxyl) and 1755 cm.$^{-1}$ (broad band). With alkaline hydrogen peroxide the compound (X) was cleaved to a carboxylic acid (XI), the constitution of which followed when it was obtained also by opening the lactone ring of the lactol (VIII) with alkali.

Brief treatment of lumisantonin with hydrogen bromide in acetic acid afforded a non-conjugated *cyclo*pentenone (XII). This gave infrared bands (in CCl_4) at 1792 (γ-lactone), 1752 (βγ-unsaturated *cyclo*pentenone), and (in Nujol) at 1627, 802, 752, and 722 cm.$^{-1}$ (triply substituted ethylenic linkage). On treatment with boiling pyridine this product (XII) furnished a new non-conjugated dienone (XIII) [showing three CMe groups and infrared bands (in CCl_4) at 1792 (γ-lactone) and 1752 (βγ-unsaturated *cyclo*pentenone) and (in Nujol) at 1643, 815, 741, and 727 cm.$^{-1}$ (triply substituted double bond)] as well as



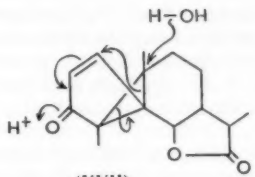
re-formed lumisantonin. The reversibility of the opening of the *cyclo*propane ring is thus demonstrated.

The bromo-ketone (XII) was unstable at room temperature: it liquefied and then resolidified to give a new conjugated dienone (XIV). The latter contained three *C*-Me groups and showed infrared bands at 1760 (γ-lactone), 1697 and 1660 (conjugated *cyclo*pentenone), and at 1630 and 722 cm.$^{-1}$ (triply substituted ethylenic linkage). The ultraviolet absorption spectrum disclosed an αβ-unsaturated ketone band at 220 mμ indicative [6] of the monosubstituted *cyclo*pentenone chromophore as shown in (XIV). On catalytic hydrogenation the ketone (XIV) readily consumed two mols. of hydrogen to give a saturated tetrahydro-ketone (XV).

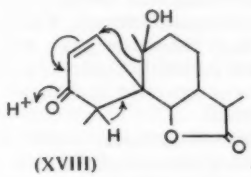
The results described above show that lumisantonin must contain the partial expression (XVI). The full formula (III) may be deduced if one considers also the following readily occurring rearrangements of lumisantonin. Treatment with acetic acid containing a trace of perchloric acid afforded the 10-acetoxy-compound (cf. II). As mentioned above,

[5] Jones and Sandorfy in Weissberger's "Technique of Organic Chemistry," Vol. IX, Interscience Publ. Inc., New York, p. 456.
[6] Woodward, *J. Amer. Chem. Soc.*, 1941, **63**, 1123; 1942, **64**, 76; Gillam and West, *J.*, 1942, 486.

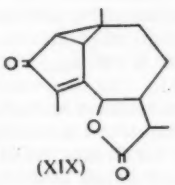
heating lumisantonin with aqueous acetic acid gave the 10-hydroxy-compound (II) itself. These rearrangements can be interpreted as in (XVII) * or as involving an intermediate (XVIII) which undergoes further rearrangement as indicated. The mild acid conditions required make the latter possibility somewhat improbable. It is of interest that opening of the *cyclo*propane ring by hydrogen bromide (see above), although leading to a different carbon skeleton, involves the same $C_{(5)} : C_{(10)}$ electron pair. With hydrogen bromide this electron pair becomes part of a π-bond system whereas with aqueous acetic acid it moves to establish a new carbon–carbon bond.



(XVII)



(XVIII)



(XIX)

By the irradiation of santonin in various solvents under different conditions the products obtained may be varied. The following facts are significant. Irradiation in hot aqueous acetic acid [1] gives the lactone (II). Irradiation in cold (0°) aqueous acetic acid affords equal amounts of this and of photosantonic acid. Lumisantonin (III) affords the lactone (II) with hot aqueous acetic acid, but is stable in the cold solvent. This suggests that there is a direct route from santonin to the lactone (II) not *via* lumisantonin, as well as a probable thermal route [3] through lumisantonin. In agreement, irradiation of lumisantonin in the cold gives photosantonic acid but no lactone (II).

It is possible, therefore, that irradiation of santonin gives an " activated state " which may collapse to lumisantonin or to the lactone (II) depending on the conditions of the experiment (temperature, acidity, etc.). The lumisantonin may then be transformed photochemically into photosantonic acid (or photosantonin) or thermally to the lactone (II). At present we visualise only the one route for the formation of photosantonic acid.

Professors Büchi and Jeger have been kind enough to send us a copy of their interesting paper on lumisantonin.[8] This provides independent evidence of the correctness of the constitution (III) and is so interpreted. Professor Cocker has also kindly sent us the proofs of his paper [9] on the same subject. The latter provides valuable experimental facts which we consider, when correctly viewed, to provide support for formula (III). The constitution (XIX) proposed by Cocker and his collaborators [9] does not comply with the evidence reported in the present paper. In particular it does not contain the system CO·CH:CH.

Experimental

$[\alpha]_D$ are in $CHCl_3$ unless stated otherwise; ultraviolet absorption spectra refer to EtOH solution. Infrared spectra were kindly determined by Dr. G. Eglinton and his colleagues, for Nujol mulls unless specified to the contrary. The silica for chromatography was supplied by B.D.H.; the term light petroleum refers to the fraction of b. p. 40—60°.

Lumisantonin.—Santonin (14 g.) in absolute ethanol (600 ml.) was irradiated in a Pyrex flask under reflux with a 125 w Crompton bare-arc mercury lamp. The progress of the

* We are grateful to Professor R. B. Woodward (Harvard) for pointing out that the rearrangement could be regarded equally as proceeding through a *cyclo*butonium ion.[7]

[7] See Roberts and Mazur, *J. Amer. Chem. Soc.*, 1951, **73**, 3542; Woodward and Kovach, *ibid.*, 1950, **72**, 1009.

[8] Arigoni, Bosshard, Bruderer, Büchi, Jeger, and Krebaum, *Helv. Chim. Acta*, 1957, **40**, 1732.

[9] Cocker, Crowley, Edward, McMurry, and Stuart, *J.*, 1957, 3416.

XUM

reaction was followed by the growth of an infrared peak at 1707 cm.$^{-1}$. Previous studies had shown that the best yield was obtained if the reaction was interrupted when this peak was, with the exception of the lactone carbonyl band, the strongest present in the carbonyl region of the spectrum. Isolation of the product and chromatography over silica gel (500 g.) gave, after elution with benzene–light petroleum (1 : 1) and crystallisation from the same solvents, *lumisantonin* (III) (1·8 g.), m. p. 153—155°, $[\alpha]_D$ −169° (*c* 1·2), $\lambda_{max.}$ 239 mμ (ε 5800) (Found: C, 73·3; H, 7·1; *C*-Me, 14·9. $C_{15}H_{18}O_3$ requires C, 73·15; H, 7·35; 3*C*-Me, 18·3%). Elution of the column with benzene–light petroleum (1 : 4) then afforded, after crystallisation (from carbon tetrachloride–light petroleum), photosantonin (2·0 g.), m. p. 67—68·5°, $[\alpha]_D$ −121° (*c* 1·3 in EtOH).

Dihydrolumisantonin.—Lumisantonin (50 mg.) in ethyl acetate (5 ml.) was hydrogenated in the presence of 5% palladised charcoal (50 mg.), 1 mol. of hydrogen being absorbed. Crystallisation from ethyl acetate–light petroleum gave *dihydrolumisantonin* (IV), m. p. 160—162°, $[\alpha]_D$ −59° (*c* 0·9), $\lambda_{max.}$ 214 mμ (ε4600) (Found: C, 72·95; H, 7·75. $C_{15}H_{20}O_3$ requires C, 72·55; H, 8·1%). The compound was recovered unchanged under the ozonolytic conditions used for the degradation of lumisantonin.

Ozonolysis of Lumisantonin.—Lumisantonin (200 mg.) in chloroform (600 ml.) was ozonised at −25° for 25 min. (until disappearance of the max. at 239 mμ). Steam-distillation afforded 0·4 mol. of formic acid [identified by the infrared spectrum of its sodium salt (KCl disc)] but no acetic acid. Isolation of the residue from the steam-distillation, and crystallisation from water, gave the *lactol* (X), m. p. 86—89°, $[\alpha]_D$ −20° (*c* 1·2) [Found: C, 60·85; H, 6·35%; equiv. (by titration), 147. $C_{15}H_{18}O_6$ requires C, 61·2; H, 6·15%; equiv. (for 2 acidic functions), 147].

Action of Hydrogen Peroxide on the Lactol (X).—The lactol (53 mg.) in ethanol (10 ml.) containing 4N-aqueous sodium hydroxide (2 ml.) was treated with 30% hydrogen peroxide (3 ml.) and set aside for 20 min. Working up in the usual way and crystallisation from acetone–light petroleum gave the *carboxylic acid* (XI), m. p. 195—200° (decomp.), $[\alpha]_D$ +59° (*c* 0·87 in EtOH) (Found: C, 58·9; H, 6·8. $C_{14}H_{20}O_6$ requires C, 59·15; H, 7·1%).

Reaction of Lumisantonin (III) *with Osmium Tetroxide.*—Lumisantonin (400 mg.) and osmium tetroxide (540 mg.) in dry dioxan (5 ml.) were set aside for 5 days. Decomposition of the complex with hydrogen sulphide and crystallisation of the product from methanol–chloroform–light petroleum gave the *diol* (VII), m. p. 178—183° (decomp.), $[\alpha]_D$ +35° (*c* 1·11), $\lambda_{max.}$ 214 mμ (ε 4200) (Found: C, 64·25; H, 7·1. $C_{15}H_{20}O_5$ requires C, 64·25; H, 7·2%).

Periodic Acid Cleavage and Hydrolysis of the Diol (VII).—The diol (150 mg.) in ethanol (25 ml.) was treated with 0·05N-aqueous periodic acid (80 ml.) and kept for 2 hr. (consumption of 2·2 atoms of oxygen). Isolation of the product and crystallisation from chloroform–light petroleum afforded the cleavage *product* (VIII), m. p. 127—129° with solidification and remelting at 172—173°, $[\alpha]_D$ −25° (*c* 0·85) (Found: C, 63·15; H, 6·6. $C_{14}H_{18}O_5$ requires C, 63·15; H, 6·8%). The substance gave a positive Fehling's test.

The product (VIII) (46 mg.) in ethanol (2·5 ml.) containing 4N-aqueous sodium hydroxide (1 ml.) was kept at room temperature for 30 min. Isolation of the product in the usual way and crystallisation from chloroform–light petroleum afforded the acid (XI), identified by m. p., mixed m. p., and infrared spectrum.

Oxidation of the Cleavage Product (VIII).—The substance (47 mg.) in acetic acid (10 ml.) was treated with sodium dichromate (67 mg.) and set aside for 22 hr. (uptake of 1 atom of oxygen). Isolation of the product in the usual way gave the *anhydride* (IX) as a glass which was purified by sublimation at 150°/10^{-4} mm.; it then melted over the range 66—69° and had $[\alpha]_D$ −105° (*c* 1·13) [Found: C, 63·35; H, 6·3%; equiv., 96·5. $C_{14}H_{16}O_5$ requires C, 63·6; H, 6·1%; equiv. (as tribasic acid), 84·8].

Formation of 10-*Hydroxy*-3-*oxoguai*-4-*en*-6 : 12-*olide* (II).—Lumisantonin (50 mg.) in 45% acetic acid (3 ml.) was refluxed in the dark for 3 hr. (no further change in $[\alpha]_D$). Crystallisation of the product from ethyl acetate–light petroleum gave the guaianolide (II) (20 mg.), m. p. and mixed m. p. 165—167°, having the same infrared spectrum as an authentic specimen.

Formation of 10-*Acetoxy*-3-*oxoguai*-4-*en*-6 : 12-*olide*.—Lumisantonin (102 mg.) in acetic acid (5 ml.) was treated with 70% perchloric acid (0·05 ml.). After 18 min. isolation of the product, chromatography over silica gel (4 g.), elution with benzene, and crystallisation from ethyl acetate–light petroleum gave the required acetate, m. p. 175—177° identical with an authentic sample prepared by the method of Cannizzaro and Fabris.[19]

[19] Cannizzaro and Fabris, *Ber.*, 1886, **19**, 2261.

Reaction of Dihydrolumisantonin with Acetic Acid.—Dihydrolumisantonin (IV) (200 mg.) in 45% acetic acid (17 ml.) was refluxed for 6 hr. (no further change in rotation). Isolation of the product, chromatography over silica gel (7 g.), elution with benzene, and crystallisation from chloroform–light petroleum gave the *ketone* (V), m. p. 192—202° (decomp.), $[\alpha]_D$ +53° (*c* 0·93), $\lambda_{max.}$ 208 mμ (ε 1900) (Found: C, 72·35; H, 8·15; *C*-Me, 17·03. $C_{15}H_{20}O_3$ requires C, 72·55; H, 8·1; 3*C*-Me, 18·15%).

Elution of the column with benzene–ether (4 : 1) and crystallisation from chloroform–light petroleum gave the hydroxy-ketone (VI), m. p. 183—204° (decomp.), $[\alpha]_D$ +106° (*c* 1·00) (Found: C, 67·35; H, 8·5. $C_{15}H_{22}O_4$ requires C, 67·65; H, 8·35%).

Reaction of Lumisantonin with Hydrogen Bromide.—Lumisantonin (100 mg.) in benzene (2 ml.) was treated with 5 drops of a 50% w/v solution of hydrogen bromide in acetic acid, and the mixture kept for 5 min. After isolation in the usual way the product was crystallised from ethyl acetate–light petroleum, to give the *bromo-ketone* (XII), m. p. 111—114°, $[\alpha]_D$ −130° (*c* 1·45) (Found: C, 55·6; H, 6·25; Br, 24·2. $C_{15}H_{19}O_3Br$ requires C, 55·55; H, 5·85; Br, 24·4%).

Spontaneous Decomposition of the Bromo-Ketone (XII).—When kept at room temperature, the bromo-ketone (150 mg.) liquefied after 2 days and then gradually (*ca.* 1 week) crystallised. The product was chromatographed over silica gel (6 g.). Elution with benzene–light petroleum (3 : 1) gave, on crystallisation from carbon tetrachloride–light petroleum, the *dienone* (XIV), m. p. 128—130°, $[\alpha]_D$ −168° (*c* 1·62), $\lambda_{max.}$ 220 mμ (ε 10,850) (Found: C, 72·95; H, 7·35; *C*-Me, 16·8. $C_{15}H_{18}O_3$ requires C, 73·15; H, 7·35; 3*C*-Me, 18·3%).

The dienone (XIV) (46·7 mg.) in ethyl acetate (5 ml.) was hydrogenated over 5% palladised charcoal (32 mg.), 2 mol. of hydrogen being absorbed. Isolation of the product and crystallisation from light petroleum gave the saturated *ketone* (XV), m. p. 62—65°, $[\alpha]_D$ −114° (*c* 1·16) (Found: C, 71·95; H, 8·56. $C_{15}H_{22}O_3$ requires C, 71·95; H, 8·85%).

Reaction of the Bromo-Ketone (XII) *with Pyridine.*—The bromo-ketone (300 mg.) in pyridine (15 ml.) was refluxed for 6 hr. Isolation of the product, chromatography over silica gel (12 g.), elution with benzene–light petroleum (1 : 1), and crystallisation from ethyl acetate–light petroleum, yielded the *dienone* (XIII), m. p. 181—183°, $[\alpha]_D$ −200° (*c* 0·74) (Found: C, 73·0; H, 6·8; *C*-Me, 14·6. $C_{15}H_{18}O_3$ requires C, 73·15; H, 7·35; 3*C*-Me, 18·3%). Further elution of the column with benzene gave lumisantonin (III), identified by m. p., mixed m. p., rotation {$[\alpha]_D$ +165° (*c* 0·87)}, and infrared spectrum.

Cold Irradiation of Santonin.—Santonin (1·0 g.) in 45 : 55 (v/v) acetic acid–water (50 ml.) was irradiated between −5° to +5° for 1½ hr. The product was separated into acidic and neutral fractions. Both were chromatographed over silica, to give photosantonic acid (180 mg.) and 10-hydroxy-3-oxoguai-4-en-6 : 12-olide (II) (196 mg.), respectively.

Cold Irradiation of Lumisantonin (III).—Lumisantonin (500 mg.) was dissolved in acetic acid (12 ml.), and the mixture then diluted with water (14 ml.). Irradiation of the mixture at −5° to +5° for 1·5 hr., followed by isolation of the acidic portion in the usual way and crystallisation from chloroform–light petroleum, afforded photosantonic acid (350 mg.), identified by m. p. and mixed m. p. No *iso*photosantonic lactone could be isolated by chromatography.

We thank the Government Grants Committee of the Royal Society and Imperial Chemical Industries Limited for financial assistance.

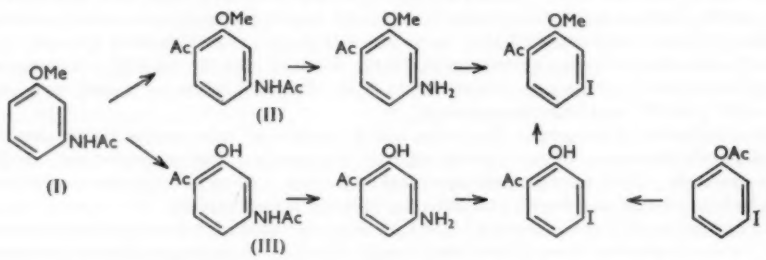
THE UNIVERSITY, GLASGOW, W.2. [*Received, July 26th,* 1957.]

30. *Synthesis of 7-Halogenoflavone and Related Compounds.*

By F. C. Chen and C. T. Chang.

From 4-halogeno-2-hydroxyacetophenone as starting material, 7-iodo-, 7-bromo-, and 7-chloro-flavanone, -flavone, and -flavonol and the corresponding chalcones have been prepared for the first time except 7-chloroflavone. The Friedel–Crafts reaction with aceto-*m*-anisidide and the Fries rearrangement of ethyl *m*-halogenophenylacetate have been more thoroughly investigated. A convenient technique for the preparation of 4-halogeno-2-hydroxyacetophenone from *m*-halogenophenyl acetate is devised.

Our interest in the synthesis of bisflavonoids, to which class belongs the structure postulated for ginkgetin by Nakazawa[1] and assigned recently to sciadopitysin,[2] kayaflavone, sotetsuflavone, and hinokiflavone by Kariyone and his collaborators,[3] led us to investigate the halogenoflavones. Since 4-halogeno-2-hydroxyacetophenone was required for the synthesis of 7-halogenoflavones in previous papers, we described its preparation by (i) Fries rearrangement of *m*-halogenophenyl acetates[4] and (ii) diazotisation of 4-amino-2-hydroxyacetophenone, followed by the replacement of the diazonium group with a halogen atom.[5] Owing to the difference of the melting points of the 2-hydroxy-4-iodoacetophenone (53—54°) obtained by the method (i) from that of the Friedel–Crafts product (69—70°) the product (m. p. 91°), obtained by the Friedel–Crafts reaction from aceto-*m*-anisidide and its de-acetylated derivative (m. p. 122—123°) (described as 4-acetamido- and 4-amino-2-hydroxyacetophenone respectively by Gibson and Levin[6]) have been revised to the 2-methoxy-structure (cf. Julia and Baillarge[7]).



In this communication a further investigation on the Friedel–Crafts reaction on aceto-*m*-anisidide, Fries rearrangement of *m*-halogenophenyl acetate and the synthesis of 7-halogeno-flavanone, -flavone, -flavonol and corresponding chalcone have been made.

It is now found that a Friedel–Crafts reaction of aceto-*m*-anisidide (I) with acetyl chloride in carbon disulphide at *ca.* 50° afforded 4-acetamido-2-methoxy- (II) (60%) and 4-acetamido-2-hydroxy-acetophenone (III) (10%), but at *ca.* 90° gave 55% of the phenol (III) with a minute yield of the ether (II). The other reactions illustrated prove the structures.

The products (II) and (III), on being dried *in vacuo* at 60°, have m. p. 135—136° and 146—147° respectively, but the melting points are variable unless precautions are taken to remove the solvent by heat. The melting points of (II) observed by Gibson and Levin (91°) and by Julia and Baillarge (87°) may be due to the retention of solvents.

[1] Nakazawa, *J. Pharm. Soc. Japan*, 1941, **61**, 174, 228.
[2] Kariyone and Kawano, *ibid.*, 1956, **76**, 448, 451, 453, 457.
[3] Kariyone and Sawada, "Complete Publication in Memory of Prof. T. Kariyone," 1956, p. 16.
[4] Chen and Chang, *J. Taiwan Pharm. Assoc.*, 1952, **4**, 38.
[5] *Idem*, *J. Chinese Chem. Soc.*, 1954, Series II, *I*, 159.
[6] Gibson and Levin, *J.*, 1931, 2402.
[7] Julia and Baillarge, *Bull. Soc. chim. France*, 1952, 639.

Fries rearrangement of *m*-chloro-, *m*-bromo-, and *m*-iodo-phenyl acetate gave the 4-halogeno-2-hydroxyacetophenones, usually in good yield. The products and their methyl ethers were identical with the compounds prepared by Friedel–Crafts reactions.

By condensation with benzaldehyde 4-halogeno-2-hydroxyacetophenones gave the halogenochalcones, which underwent ring closure to 7-halogenoflavanones. These were dehydrogenated by *N*-bromosuccinimide,[8] yielding 7-halogenoflavones [4] which were also obtained by the action of selenium dioxide in pentyl alcohol on the corresponding chalcones, according to Venkataraman's method.[9] Algar–Flynn oxidation [10] of the chalcone, or Oyamada's method [11] with hydrogen peroxide in methanolic sodium hydroxide, gave the 7-halogenoflavonols in good yield.[12] The only known compound of this class appears to be 7-chloroflavone.[13] The chloro-, bromo-, and iodo-substituted members of these various series, as well as the 4'-methoxy-compounds, have been prepared, and preparation of the fluoro-compounds is being studied.

Experimental

Ethanol was used for crystallisation unless otherwise stated.

*Friedel–Crafts Reaction of Aceto-*m*-anisidide.*—(a) *Acetylation at* 50—60°. To an ice-cooled solution of aceto-*m*-anisidide (3 g.) and acetyl chloride (3·5 g.) in dry carbon disulphide (10 c.c.) was added anhydrous aluminium chloride (9 g.) in portions, with stirring, during about 10 min. The mixture was stirred at room temperature for 30 min., then heated at 50—60° for 1·5 hr. After decomposition with ice-water the yellow product was collected and extracted with 10% aqueous potassium hydroxide. The alkali-insoluble product was washed with cold benzene (to remove oil) and crystallised from 30% aqueous alcohol (charcoal) as colourless needles (2·1 g.) of 4-acetamido-2-methoxyacetophenone dihydrate, shrinking at *ca.* 80° and melting at 132°. When dried previously at 50—60°/1 mm. it melted consistently at 135—136° (lit., 91°,[6] 87° [7]) (Found: C, 63·5; H, 6·5; N, 6·8. Calc. for $C_{11}H_{13}O_3N$: C, 63·7; H, 6·3; N, 6·8. Found: loss at 60° *in vacuo*, 14·8. Calc. for $C_{11}H_{13}O_3N,2H_2O$: loss, 14·9%).

The alkali-soluble portion obtained in the above separation, on acidification with acetic acid, gave 4-acetamido-2-hydroxyacetophenone monohydrate, which formed colourless needles from 30% aqueous alcohol. It melted partially at *ca.* 105°, but did not clear till 110°, resolidified at 117°, and remelted at 141—142°. When dried previously or rapidly crystallised from anhydrous benzene it gave colourless crystals (0·4 g.), m. p. 146—147° (lit., 142°,[14] 142—144° [15]) (Found: C, 62·0; H, 5·9; N, 7·3. Calc. for $C_{10}H_{11}O_3N$: C, 62·2; H, 5·7; N, 7·2. Found: loss at 60°/1 mm.: 8·8. Calc. for $C_{10}H_{11}O_3N,H_2O$: loss, 8·9%).

(b) *Acetylation at* 80—90°. To a solution of aceto-*m*-anisidide (8 g.) and acetyl chloride (10 c.c.) in dry carbon disulphide (25 c.c.), aluminium chloride (24 g.) was added in small portions with stirring, and the mixture kept at 80—90° for 1·5 hr. The product was worked up as described above. It consisted mainly of alkali-soluble 4-acetamido-2-hydroxyacetophenone (5·1 g.), with only a minute yield of 4-acetamido-2-methoxyacetophenone.

4-Acetamido-2-methoxyacetophenone (2 g.) was boiled with 15% hydrochloric acid (4 c.c.) for 20 min. Neutralisation with aqueous ammonia afforded 4-amino-2-methoxyacetophenone (1·2 g.), needles, m. p. 121—122° (lit.,[7] 122—123°) (Found: C, 65·4; H, 6·8; N, 8·6; OMe, 19·0. Calc. for $C_9H_{11}O_2N$: C, 65·5; H, 6·6; N, 8·5; 1OMe, 18·9%).

4-Amino-2-hydroxyacetophenone.—4-Acetamido-2-hydroxyacetophenone (4 g.) was boiled with 15% hydrochloric acid (7 c.c.) for 15 min., as described above, giving 4-amino-2-hydroxyacetophenone (2·7 g.), lemon-yellow needles, m. p. 129—130° (lit.,[7] 130°) (Found: C, 63·8; H, 6·1; N, 9·5. Calc. for $C_8H_9O_2N$: C, 63·6; H, 5·9; N, 9·3%).

4-Iodo-2-methoxyacetophenone.—4-Amino-2-methoxyacetophenone (0·5 g.) in water (10 c.c.) and concentrated sulphuric acid (1 c.c.; *d* 1·82) was diazotised at 0° with sodium nitrite (0·3 g.)

[8] Chen, *J. Taiwan Pharm. Assoc.*, 1951, **3**, 9.
[9] Mahal, Rai, and Venkataraman, *J.*, 1935, 866; 1936, 569.
[10] Algar and Flynn, *Proc. Roy. Irish Acad.*, 1934, *B*, **42**, 1.
[11] Oyamada, *J. Chem. Soc. Japan*, 1934, **55**, 1256.
[12] Chen and Shu, *J. Taiwan Pharm. Assoc.*, 1953, **5**, 49.
[13] Cramer and Elschnig, *Chem. Ber.*, 1956, **89**, 1.
[14] Bapat and Venkataraman, *Proc. Indian Acad. Sci.*, 1955, **49**, *A*, 336.
[15] Feldman and Simeonov, *Zhur. obshchei Khim.*, 1953, **23**, 2043.

in water (1 c.c.) during 5 min. After a further 10 minutes' stirring, potassium iodide (0·7 g.) in water (2 c.c.) and copper bronze (0·05 g.) were added. Then the temperature was slowly raised and kept at 75—80° until no more nitrogen was evolved. The resulting mixture was cooled and extracted with chloroform. The chloroform layer was washed with water and steam-distilled. After the chloroform a slightly reddish product was obtained from the distillate, this was decolorised by sodium thiosulphate solution, giving colourless needles (0·45 g.) of the *iodo-compound*, m. p. 69—70° (Found: C, 39·3; H, 3·5; I, 47·8; OMe, 11·0. $C_9H_9O_2I$ requires C, 39·1; H, 3·3; I 46·0; 1OMe, 11·2%).

2-Hydroxy-4-iodoacetophenone.—4-Amino-2-hydroxyacetophenone (0·5 g.), treated as above, yielded *2-hydroxy-4-iodoacetophenone* (0·4 g.), needles, m. p. 53—54° (Found: C, 36·5; H, 2·9; I 50·2. $C_8H_7O_2I$ requires C, 36·5; H, 2·7; I, 48·4%).

Fries Rearrangement of m-*Halogenophenyl Acetates.*—(1) *2-Hydroxy-4-iodoacetophenone*: (*a*) In chlorobenzene. To *m*-iodophenyl acetate (10·5 g.) in redistilled chlorobenzene (52 c.c.) anhydrous aluminium chloride (7 g.) was added quickly. The mixture was stirred and kept at 125—135° for 4·5 hr. The mixture was cooled and the complex decomposed by ice-water and then made alkaline with 10% aqueous sodium hydroxide. The solution was steam-distilled, then made slightly acidic with hydrochloric acid, and steam-distilled again. The product from the distillate crystallised in colourless prisms (6·8 g., 64%), m. p. 53—54°, identical with the product from the Friedel–Crafts reaction.

(*b*) In nitrobenzene. *m*-Iodophenyl acetate (13 g.) and anhydrous aluminium chloride (6 g.) in nitrobenzene (100 c.c.) were treated at 140° for 4 hr., then decomposed with ice-water and dilute hydrochloric acid. The mixture was washed with water and extracted with 10% aqueous potassium hydroxide. The extract was slightly acidified and steam-distilled. The colourless product from the distillate crystallised in prisms (5·5 g., 42%), m. p. 53—54°.

This phenol (0·1 g.), anhydrous potassium carbonate (0·1 g.), and excess of methyl iodide (0·8 g.) in acetone (2 c.c.) were refluxed for 8 hr. The excess of methyl iodide and acetone was distilled off and the residue washed with 5% aqueous potassium hydroxide and with water. Crystallisation gave needles (0·08 g.), m. p. 69—70°, alone or mixed with a specimen obtained from the Friedel–Crafts reaction.

(2) *4-Bromo-2-hydroxyacetophenone.* *m*-Bromophenyl acetate (29 g.) and aluminium chloride (60 g.), heated at 170° for 3 hr., then decomposed with dilute hydrochloric acid and steam-distilled, gave the *ketone* (25·5 g.), m. p. 42—43° (Found: C, 44·6; H, 3·4; Br, 37·0. $C_8H_7O_2Br$ requires C, 44·8; H, 3·2; Br, 37·2%).

(3) *4-Chloro-2-hydroxyacetophenone.* *m*-Chlorophenyl acetate (6·8 g.) and aluminium chloride (12·7 g.) were heated at 175—180° for 1·5 hr. The mixture was treated with hydrochloric acid and steam-distilled. The distillate was extracted with chloroform, and the combined extracts were re-extracted with 10% aqueous potassium hydroxide. Then the combined aqueous alkaline solution was washed with chloroform, acidified, and extracted with chloroform again. Removing solvent gave a pale orange liquid which was dried in a desiccator and purified by vacuum-distillation, giving a colourless oil (5·8 g., 85%), b. p. 121—124/15 mm. (lit.,[13] 126°/16 mm.).

Synthesis of 4'-Halogeno-2'-hydroxychalcones.—*2'-Hydroxy-4'-iodochalcone.* To a cooled mixture of 2-hydroxy-4-iodoacetophenone (1 g.) and benzaldehyde (0·8 g.) in alcohol (12 c.c.) was added cold 60% aqueous potassium hydroxide (11 c.c.). The mixture was securely stoppered and kept at 0° for 2 days with occasional shaking. The mixture was diluted with water and acidified with dilute hydrochloric acid. The precipitated *chalcone* was collected and crystallised, giving yellow needles (1·1 g.), m. p. 112—113° (Found: C, 51·2; H, 3·3; I, 37·5. $C_{15}H_{11}O_2I$ requires C, 51·4; H, 3·1; I, 36·2%).

Similarly were prepared *4'-bromo-2'-hydroxychalcone*, needles (87%), m. p. 115—116° (Found: C, 59·8; H, 3·8; Br, 26·1. $C_{15}H_{11}O_2Br$ requires C, 59·4; H, 3·6; Br, 26·3%), *4'-chloro-2'-hydroxychalcone*, needles (77%), m. p. 124—125° (Found: C, 69·4; H, 4·4; Cl, 13·9. $C_{15}H_{11}O_2Cl$ requires C, 69·6; H, 4·2; Cl, 13·7%), *2'-hydroxy-4'-iodo-4-methoxychalcone*, needles (73%), m. p. 161—162° (Found: C, 50·3; H, 3·6; I, 34·7; OMe, 7·9. $C_{16}H_{13}O_3I$ requires C, 50·5; H, 3·4; I, 33·4; OMe, 8·1%), *4'-bromo-2'-hydroxy-4-methoxychalcone*, needles (84%), m. p. 136—137° (Found: C, 57·3; H, 4·2; Br, 24·4; OMe, 9·0. $C_{16}H_{13}O_3Br$ requires C, 57·6; H, 3·9; Br, 24·0; OMe, 9·3%), and *4'-chloro-2'-hydroxy-4-methoxychalcone*, orange needles (80%), m. p. 136—137° (Found: C, 66·2; H, 4·8; Cl, 12·5; OMe, 10·4. $C_{16}H_{13}O_3Cl$ requires C, 66·5; H, 4·5; Cl, 12·3; OMe, 10·7%).

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Syntheses of 7-*Halogenoflavanones.*—(1) 7-*Iodoflavanone.* A solution of 2′-hydroxy-4′-iodochalcone (1 g.) and phosphoric acid (*d* 1·75; 4·5 c.c.) in alcohol (150 c.c.) was refluxed for 48 hr. Concentration the solution (to 50 c.c.) gave colourless needles (0·5 g.), m. p. 114—115° (Found: C, 51·1; H, 3·4; I, 37·6. $C_{15}H_{11}O_2I$ requires C, 51·4; H, 3·1; I, 36·2%).

(2) 7-*Bromoflavanone.* A solution of 4′-bromo-2′-hydroxychalcone (2·5 g.) and phosphoric acid (*d* 1·75; 10 c.c.) in alcohol (375 c.c.) was refluxed for 72 hr. The solution was concentrated to about 70 c.c. and cooled. Unchanged chalcone was then precipitated and decanted. The *flavanone* crystallised as colourless needles (1 g.), m. p. 79—80° (Found: C, 59·1; H, 3·9; Br, 26·7. $C_{15}H_{11}O_2Br$ requires C, 59·4; H, 3·6; Br, 26·3%).

(3) 7-*Chloroflavanone.* To 4′-chloro-2′-hydroxychalcone (1·5 g.) in alcohol (150 c.c.) phosphoric acid (*d* 1·75; 6·5 c.c.) was added. The mixture was refluxed for 72 hr., then after concentration gave the *flavanone* as needles, m. p. 54—55·5° (Found: C, 69·3; H, 4·6; Cl, 13·9. $C_{15}H_{11}O_2Cl$ requires C, 69·6; H, 4·3; Cl, 13·7%).

(4) 7-*Iodo*-4′-*methoxyflavanone.* 2′-Hydroxy-4′-iodo-4-methoxychalcone (1 g.) and phosphoric acid (*d* 1·75; 4·5 c.c.) in alcohol (150 c.c.), as above, gave the *flavanone* as needles (from dioxan), m. p. 166·5—167·5° (Found: C, 50·2; H, 3·6; I, 34·4; OMe, 8·0. $C_{16}H_{13}O_3I$ requires C, 50·5; H, 3·4; I, 33·4; OMe, 8·1%).

(5) 7-*Bromo*-4′-*methoxyflavone,* prepared from 4′-bromo-2′-hydroxy-4-methoxychalcone as above, formed needles, m. p. 130—130·5° (Found: C, 57·4; H, 4·1; Br, 22·5; OMe, 9·1. $C_{16}H_{13}O_3Br$ requires C, 57·7; H, 3·9; Br, 23·9; OMe, 9·3%.

Synthesis of 7-*Halogenoflavones.*—(1) 7-*Iodoflavone.* (*a*) With selenium dioxide. A mixture of 2′-hydroxy-4′-iodochalcone (1 g.), selenium dioxide (1 g.), and pentyl alcohol (14 c.c.) was refluxed for 10 hr. The precipitated selenium was then filtered off and washed with hot ethanol, and the filtrate was subjected to steam-distillation. After the removal of pentyl alcohol, the solid *flavone* was collected and crystallised from 75% aqueous dioxan, giving colourless needles (0·6 g.), m. p. 167—168° (Found: C, 51·5; H, 2·8; I, 37·5. $C_{15}H_9O_2I$ requires C, 51·7; H, 2·6; I, 36·4%).

(*b*) With *N*-bromosuccinimide. 7-Iodoflavanone (0·1 g.) and *N*-bromosuccinimide (0·07 g.) in carbon tetrachloride (10 c.c.) were refluxed for 1 hr., during which a transient red colour appeared, then faded. After cooling, the mixture was filtered, the filtrate evaporated, and the residual product crystallised, to give 7-iodoflavone (70 mg.), m. p. 168—169°, identical with the preceding product.

(2) 7-*Bromoflavone.* Reactions as in (*a*) or (*b*) above gave this *flavone* which crystallised from alcohol and finally from dioxan, as needles, m. p. 167—168° (Found: C, 59·5; H, 3·3; Br, 26·9. $C_{15}H_9O_2Br$ requires C, 59·8; H, 3·0; Br, 26·5%) [(*a*) 1·94 g. from 3·0 g., (*b*) 55 mg. from 0·12 g.

(3) 7-*Chloroflavone.* 4′-Chloro-2′-hydroxychalcone (1·6 g.), selenium dioxide (1·5 g.), and pentyl alcohol (23 c.c.) were treated, as above, giving colourless needles (0·73 g.), m. p. 156—157° (lit.,[13] 158°) (Found: C, 69·7; H, 3·7; Cl, 13·5. Calc. for $C_{15}H_9O_2Cl$: C, 70·1; H, 3·5; Cl, 13·8%).

(4) 7-*Bromo*-4′-*methoxyflavone* was prepared from 4′-bromo-2′-hydroxy-4-methoxychalcone (2 g.), selenium dioxide (2 g.), and pentyl alcohol (35 c.c.), as needles (0·9 g.), m. p. 184—185° (Found: C, 58·4; H, 3·7; Br, 23·8; OMe, 9·8. $C_{16}H_{11}O_3Br$ requires C, 58·0; H, 3·3; Br, 24·1; OMe, 9·5%).

(5) 7-*Chloro*-4′-*methoxyflavone,* prepared from 4′-chloro-2′-hydroxy-4-methoxychalcone (1 g.), selenium dioxide (1 g.), and pentyl alcohol (14 c.c.), formed needles (0·5 g.), m. p. 190·5—191·5° (Found: C, 66·6; H, 4·3; Cl, 12·5; OMe, 11·3. $C_{16}H_{11}O_3Cl$ requires C, 67·0; H, 3·9; Cl, 12·3; OMe, 10·8%).

(6) 7-*Iodo*-4′-*methoxyflavone,* from 2′-hydroxy-4′-iodo-4-methoxychalcone (1 g.), selenium dioxide (1 g.), and pentyl alcohol (14 c.c.), formed needles (0·2 g.), m. p. 205—206° (Found: C, 50·5; H, 3·2; I, 32·2; OMe, 8·5. $C_{16}H_{11}O_3I$ requires C, 50·8; H, 2·9; I, 33·6; OMe, 8·2%).

Synthesis of 7-*Halogenoflavonols.*—7-*Iodoflavonol.* 2′-Hydroxy-4′-iodochalcone (0·5 g.) was added to a mixture of methanol (15 c.c.) and 16% aqueous sodium hydroxide (2 c.c.). To the resulting solution was added dropwise 15% hydrogen peroxide (2 c.c.) with stirring and ice-cooling. After 24 hr. in a refrigerator, it was filtered and acidified with dilute hydrochloric acid, to give pale yellow prisms (0·35 g.), m. p. 188·5—189·5° (Found: C, 49·1; H, 2·9; I, 36·0. $C_{15}H_9O_3I$ requires C, 49·5; H, 2·5; I, 34·9%).

Similar reactions gave 7-*bromoflavonol,* needles, m. p. 178—179° (Found: C, 56·4; H, 3·3;

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Br, 25·5. $C_{15}H_9O_3Br$ requires C, 56·8; H, 2·9; Br, 25·2%), *7-chloroflavonol*, yellow prisms (84%), m. p. 180·5—181·5° (Found: C, 65·4; H, 3·6; Cl, 13·5. $C_{15}H_9O_3Cl$ requires C, 66·1; H, 3·3; Cl, 13·0%), *7-chloro-4'-methoxyflavonol*, pale yellow needles (82%), m. p. 192—193° (Found: C, 63·1; H, 3·6; I, 12·9; OMe, 10·6. $C_{16}H_{11}O_4Cl$ requires C, 63·5; H, 3·4; I, 11·7; OMe, 10·2%), *7-bromo-4'-methoxyflavonal*, as pale yellow needles, m.p. 193—194° (Found: C, 55·1; H, 3·5; Br, 22·8; OMe, 8·7. $C_{16}H_{11}O_4Br$ requires C, 55·3; H, 3·2; Br, 23·0; OMe, 8·9%), and *7-iodo-4'-methoxyflavonol*, as yellow needles, m. p. 206—207° (Found: C, 48·4; H, 3·0; I, 33·3; OMe, 8·2. $C_{16}H_{11}O_4I$ requires C, 48·8; H, 2·8; I, 32·2; OMe, 7·9%).

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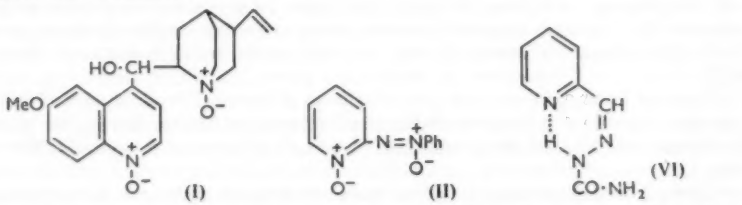
31. *N-Oxides and Related Compounds. Part VII.*[1] *Per-acid Oxidation of Some Conjugated Pyridines.*

By A. R. KATRITZKY and A. M. MONRO.

β-3- and -4-Pyridylacrylic acid and their ethyl esters and amides, 2- and 4-styrylpyridines, and pyridine-2-aldoxime and its semicarbazone gave 1-oxides with peracetic acid.

CONJUGATED pyridine 1-oxides, previously little known, were required for physical measurements. Previous work on the per-acid oxidation of pyridines containing sensitive groups showed that quinine gave successively the quinuclidine monoxide and the di-*N*-oxide (I) without affecting the isolated vinyl group.[2] but that 2-benzylthiopyridine and tri-2-pyridyl-phosphine and -arsine gave the sulphoxide,[3] phosphine oxide, and arsine oxide [4] and not *N*-oxides. 2-Phenylazopyridine gave the azoxy-oxide (II).[5] We now show that oxidation of pyridines containing conjugated carbon–carbon and carbon–nitrogen double bonds gives the 1-oxides.



β-3- and -4-Pyridylacrylic acid and the corresponding ethyl esters and amides with peracetic acid all gave single products containing one extra oxygen atom, in good yield.

[1] Part VI, Hands and Katritzky, *J.*, 1957, 4385.
[2] Ochiai, *J. Org. Chem.*, 1953, **18**, 534.
[3] Shaw, Bernstein, Losee, and Lott, *J. Amer. Chem. Soc.*, 1950, **72**, 4362.
[4] Mann and Watson, *J. Org. Chem.*, 1948, **13**, 502.
[5] Colonna and Risaliti, *Gazzetta*, 1955, **85**, 1148.

In each series the same position had been oxidised, for the esters gave the corresponding amides and acids. The products were shown to be *N*-oxides, and not epoxides, by infrared and ultraviolet spectra.[6] 2- and 4-Styrylpyridine with peracetic acid gave the corresponding *N*-oxides in poor yield, identical with the products of reaction of 2- and 4-picoline 1-oxide with benzaldehyde. 3-Pyridylacetic acid (itself readily *N*-oxidised) with benzaldehyde gave β-phenyl-α-3-pyridylacrylic acid, which it is hoped to convert into 3-styrylpyridine.

Pyridine-2-aldehyde and benzyl cyanide in conflicting reports [7,8] are stated to give compounds (III) and (IV): we obtained only the former; peracetic oxidation failed, as did that of the *O*-benzoyl derivative of pyridine-2-aldehyde cyanohydrin. Hydrogen peroxide is known to hydrolyse cyano-groups very readily [9] although both 2- [10] and 3-cyanopyridine [11] have given 1-oxides directly. In the attempted preparation of quinoline-2-aldehyde cyanohydrin, only the quinaldoin cyanohydrin (V) was obtained; a similar product in the pyridine series is known.[12]

Pyridine-1-aldehyde with peracetic acid gave successively 2-picolinic acid (oxidation to the acid has been reported in the 4-series [13]) and the corresponding 1-oxide, but pyridine-2-aldoxime and the related semicarbazone gave 1-oxides, each convertible into the dinitrophenylhydrazone oxide. A by-product, isomeric with the starting material, was isolated on oxidation of the semicarbazone. This was the *cis*-semicarbazone (VI) (known in other cases [14]) (which would be expected to be more difficult to oxidise than the predominating *trans*-isomer) for it gave pyridine-2-aldehyde 2 : 4-dinitrophenylhydrazone. Oxidation of the benzoyl derivative of the oxime gave only benzoic acid and pyridoin. 4-Acetylpyridine hydrazone and the azine were not *N*-oxidised smoothly. 3- and 4-Pyridylcarboxyhydrazide gave only the corresponding acids with peracetic acid, but the analogous *N'*-benzenesulphonylhydrazides gave 1-oxides. β-4-Pyridylpropionamide and *N*-benzyl-*iso*nicotinamide were readily *N*-oxidised.

Experimental

Oxidations with Peracetic Acid.—The pyridine (0·01 mole), aqueous 30% hydrogen peroxide (1·47 c.c.), and acetic acid (6 c.c.) were heated for 18 hr. at 70°, and volatile matter was removed at 100°/15 mm. The residue was either crystallised directly, or (if semi-solid) treated in hot chloroform (15 c.c.) with potassium carbonate (0·8 g.) and recovered from the chloroform by evaporation.

Pyridylacrylic Acid Derivatives.—The following 1-*oxides* were prepared: β-4-*pyridylacrylic acid* (50%), prisms (from pentyl alcohol), m. p. 237—240° (decomp.) (Found: C, 58·3; H, 4·5; N, 8·0. $C_8H_7O_3N$ requires C, 58·2; H, 4·3; N, 8·5%) [*hemiacetate*, plates, m. p. 237—240° (decomp.), from acetic acid (Found: C, 55·1; H, 4·8; N, 7·5. $C_8H_7O_3N,\frac{1}{2}C_2H_4O_2$ requires C, 55·4; H, 4·7; N, 7·2%)]; β-4-*pyridylacrylamide* (18%), prisms (from methanol or water), m. p. 246° (decomp.) (darkens above 235°) (Found: C, 58·7; H, 5·2. $C_8H_8O_2N_2$ requires C, 58·5; H, 4·9%); *ethyl* 2-4′-*pyridylacrylate* (51%), prisms [from benzene–light petroleum (b. p. 60—80°)], m. p. 145° (Found: C, 62·1; H, 5·5; N, 7·2. $C_{10}H_{11}O_3N$ requires C, 62·2; H, 5·7; N, 7·2%), which with 2N-aqueous sodium hydroxide during 12 hr. at 100° followed by acetic acid, gave the corresponding acid, m. p. and mixed m. p. 238—240° (decomp.), and with aqueous-methanolic ammonia in 5 days at 0° gave the amide (85%), m. p. and mixed m. p. 245° (decomp.); β-3-*pyridylacrylic acid* (95%), prisms (from acetic acid), m. p. 273—274° (decomp.,

[6] Katritzky and co-workers, unpublished work.
[7] Klosa, *Arch. Pharm.*, 1956, **289**, 177.
[8] Profft, Schneider, and Beyer, *J. prakt. Chem.*, 1955, **2**, 147.
[9] Radziszewski, *Ber.*, 1885, **18**, 355.
[10] Leonard and Wajngurt, *J. Org. Chem.*, 1956, **21**, 1077.
[11] Jujo, *J. Pharm. Soc. Japan*, 1946, **66**, 21.
[12] Mathes and Sauermilch, *Chem. Ber.*, 1956, **89**, 1515.
[13] Mathes and Sauermilch, *Chem. Ztg.*, 1952, **76**, 519.
[14] Wittig, "Stereochemie," Akademische Verlag, Leipzig, 1930, p. 200.

depends on rate of heating) (Found: C, 58·7; H, 4·5%); β-3-*pyridylacrylamide* (50%), needles [from ethanol–water (5 : 1)], m. p. 235° (decomp.) (Found: C, 59·0; H, 5·0%); *ethyl* β-3′-*pyridylacrylate* (96%), prisms (from ethyl acetate), m. p. 99—101°, also prepared (73%) by esterification with ethanol–sulphuric acid of the corresponding acid [converted (as in 4-series) into the acid (88%), m. p. and mixed m. p. 274—275° (decomp.), and the amide (71%), m. p. and mixed m. p. 235° (decomp.)] (Found: C, 61·9; H, 5·6%).

2- *and* 4-*Styrylpyridine* 1-*Oxide*.—(i) Oxidation gave the *oxide* (40%) of the 2-isomer as prisms (from benzene), m. p. 162° (Found: C, 78·9; H, 5·7; N, 7·1. $C_{13}H_{11}ON$ requires C, 79·2; H, 5·6; N, 7·1%); and the 4-isomer gave an *oxide* (28%), prisms (from ethyl methyl ketone), m. p. 169° (Found: C, 79·6; H, 5·8%).

(ii) Benzaldehyde (10·6 g.), 2-picoline 1-oxide (10·9 g.), and methanolic 5% potassium methoxide (50 c.c.) were refluxed for 3 hr. After 12 hr. more, excess of carbon dioxide was passed in, and the whole filtered and steam-distilled. 2-Styrylpyridine 1-oxide (4·3 g., 22%) crystallised from the residue and had m. p. and mixed m. p. 160°. 4-Picoline 1-oxide similarly gave 4-styrylpyridine 1-oxide (11%), m. p. and mixed m. p. 167—169°.

3-*Pyridylacetic Acid*.—Refluxing ethyl 3-pyridylacetate (20·4 g.) for 8 hr. with aqueous potassium hydroxide (11 g. in 11 c.c.) and ethanol (28 c.c.), followed by addition of aqueous 12N-hydrochloric acid (14·6 c.c.), filtration, evaporation, and extraction of the residue with methanol, gave the acid (12·5 g., 75%), m. p. 141—143° (lit.,[15] m. p. 144°) [1-*oxide* (67%), prisms (from ethyl acetate–ethanol), m. p. 142—144° (decomp.) (Found: 54·9; H, 4·7. $C_7H_7O_3N$ requires C, 54·9, H, 4·6%)].

The acid (1·27 g.), benzaldehyde (1·5 c.c.), piperidine (0·2 c.c.), and pyridine (10 c.c.), when heated for 2 days at 115° and poured into water, gave β-*phenyl*-α-3-*pyridylacrylic acid* (0·85 g., 40%), needles (from ethanol), m. p. 234—235° (slight decomp.) (Found: C, 74·8; H, 5·3; N, 6·3. $C_{14}H_{11}O_2N$ requires C, 74·7; H, 4·9; N, 6·2%).

α-*Phenyl*-β-2-*pyridylacrylonitrile*.—Aqueous 10% sodium hydroxide (0·5 c.c.) was added slowly at 0° to pyridine-2-aldehyde (1·07 g.) and benzyl cyanide (1·17 g.) in ethanol (2·0 c.c.). After 18 hr., the nitrile (1·53 g., 74%) was collected; it formed prisms, m. p. 63—66° (lit.,[7] m. p. 61—63°), from ethanol (Found: C, 81·2; H, 5·0; N, 13·3%; *M*, 185. Calc. for $C_{14}H_{10}N_2$: C, 81·5; H, 4·9; N, 13·6%; *M*, 206).

O-*Benzoyl*(*pyridine-2-aldehyde Cyanohydrin*).—This *compound* (26%) (prepared as for the oxime benzoate below), formed prisms, m. p. 102° from ethanol (Found: C, 70·1; H, 4·3; 11·7. $C_{14}H_{10}O_2N_2$ requires C, 70·6; H, 4·2; N, 11·8%). Pyridoin (12%), orange needles, m. p. 156° (lit.,[13] m. p. 156°), separated later from the aqueous mother-liquors (Found: C, 66·8; H, 4·5. Calc. for $C_{12}H_{10}O_2N_2$: C, 67·3; H, 4·7%).

1-*Cyano*-1 : 2-*di*-2′-*quinolylethane*-1 : 2-*diol*.—Aqueous sodium cyanide (0·94 g. in 2 c.c.) was slowly added at −10° to quinoline-2-aldehyde (3·14 g.) in aqueous 2N-hydrochloric acid (10 c.c.). Precipitated solid was recrystallised from benzene and from ethyl acetate, to give the *diol* (2·1 g., 62%) as brown plates, m. p. 133° (decomp.) (Found: C, 74·2; H, 4·6; N, 12·2. $C_{21}H_{16}O_2N_2$ requires C, 73·9; H, 4·4; N, 12·3%).

Pyridine-2-aldoxime Oxide and the Semicarbazone Oxide.—Oxidation gave the *aldoxime oxide* (62%), pale yellow needles (from ethanol), m. p. 222° (decomp.) (Found: C, 52·6; H, 4·5. $C_6H_6O_2N_2$ requires C, 52·2; H, 4·4%), and *semicarbazone oxide* (65%), insoluble in chloroform (chloroform-soluble by-product isolated, see below), needles (from acetic acid–ethyl acetate), m. p. 233° (decomp.) (Found: C, 46·5; H, 4·6. $C_7H_8O_2N_4$ requires C, 46·7; H, 4·5%).

Both compounds with 2 : 4-dinitrophenylhydrazine in ethanolic hydrochloric acid gave the corresponding 2 : 4-*dinitrophenylhydrazone* 1-*oxide* (55% and 35%), orange needles (from acetic acid), m. p. 285—290° (decomp.) (Found: C, 47·7; H, 2·7. $C_{12}H_9O_5N_5$ requires C, 47·7; H, 3·0%).

Extraction of crude pyridine-2-aldehyde semicarbazone 1-oxide with chloroform gave (from the chloroform) the cis-*semicarbazone* (3%), prisms (from ethanol), m. p. 158° (Found: C, 51·0; H, 4·8. $C_7H_8ON_4$ requires C, 51·2; H, 4·9%).

On treatment with ethanolic hydrochloric acid and 2 : 4-dinitrophenylhydrazine, both *cis*- and normal (*i.e.*, mainly *trans*-)pyridine-2-aldehyde semicarbazone gave the 2 : 4-dinitrophenylhydrazone (84% and 60%), m. p. 226—228°, identical with an authentic specimen (lit.,[16] m. p. 229°).

[15] Hartmann and Bosshard, *Helv. Chim. Acta*, 1941, **24**, 28E.
[16] Grammaticakis, *Bull. Soc. chim. France*, 1956, 109.

O-*Benzoyl*(*pyridine-2-aldoxime*).—Benzoyl chloride (0·32 c.c.) was added slowly to pyridine-2-aldoxime (0·31 g.) in pyridine (1 c.c.) at 0°, the whole kept for 18 hr., and water added. The *benzoyl derivative* (0·45 g. 80%) formed prisms, m. p. 112·5°, from ethanol [mixed m. p. with the oxime (m. p. 112°), 85—90°] (Found: C, 69·2; H, 4·8; N, 12·0. $C_{13}H_{10}O_2N_2$ requires C, 69·0; H, 4·5; N, 12·4%).

Treatment with peracetic acid gave benzoic acid (18%) and pyridoin (40%), m. p. 152°, as the only products isolated.

4-*Acetylpyridine Derivatives*.—This ketone gave [17] the *azine* (68%), pale yellow plates [from light petroleum (b. p. 80—100°)], m. p. 125·5—127° (Found: C, 70·5; H, 5·8. $C_{14}H_{14}N_4$ requires C, 70·6; H, 5·9%). and, when heated for 1 min. with two parts of hydrazine hydrate (100%), gave the *hydrazone* (83%), plates (from benzene), m. p. 121—122° (Found: C, 62·1; H, 6·8. $C_7H_9N_3$ requires C, 62·2; H, 6·7%).

2-, 3-, *and* 4-(*N'-Benzenesulphonylhydrazinocarbonyl*)*pyridine* 1-*Oxide*.—Oxidation of the corresponding pyridine gave the 4-substituted *pyridine* 1-*oxide* (40%), needles (from water), m. p. 238—239° (decomp.; depends on heating rate) (Found: C, 49·3; H, 3·9; N, 14·0. $C_{12}H_{11}O_4N_3S$ requires C, 49·1; H, 3·8; N, 14·3%), the 3-*analogue* (44%), needles (from water or ethanol), m. p. 222—224° (decomp.) (Found: C, 48·7; H, 3·8; N, 14·1%), and the 2-*analogue* (48%), needles (from acetic acid, m. p. 209—212° (decomp.) (Found: C, 49·1; H, 4·0; N, 14·1%)

Preparation and Oxidation of Amides.—Ethyl *iso*nicotinate (5·5 g.) was refluxed for 4 hr. with benzylamine (12 c.c.). Removal of excess of amine at 100°/14 mm. then gave *N*-benzyl-*iso*nicotinamide (71%), needles (from ethyl acetate–light petroleum), m. p. 90—92° (lit.,[18] m. p. 84·5—85°); the *methotoluene*-p-*sulphonate* formed plates (from ethanol), m. p. 194·5—196·5° (Found: C, 63·1; H, 5·7. $C_{21}H_{22}O_4N_2S$ requires C, 63·3; H, 5·6%). N-2-(3-*Indolyl*)-*ethylisonicotinamide* was similarly prepared (73%) by heating the amine and ester for 10 hr. at 140° and separated from ethanol–benzene, having m. p. 165·5—167° (Found: C, 72·6; H, 5·8. $C_{16}H_{15}ON_3$ requires C, 72·4; H, 5·7%) [*methotoluene*-p-*sulphonate*, plates (from ethyl acetate–ethanol), m. p. 174—175·5° (Found: C, 63·4; H, 5·4; N, 9·3. $C_{24}H_{25}O_4N_3S$ requires C, 63·8; H, 5·6; N, 9·3%)].

Oxidation gave β-4-*pyridylpropion*- (42%), rods, m. p. 227°, from ethanol (Found: C, 57·9; H, 6·0; N, 16·6. $C_8H_{10}O_2N_2$ requires C, 57·8; H, 6·1; N, 16·9%), and N-*benzylisonicotin-amide* 1-*oxide* (66%), prisms (from ethanol), m. p. 184° (Found: C, 68·4; H, 5·0. $C_{13}H_{12}O_2N_2$ requires C, 68·4; H, 5·3%).

This investigation was carried out during the tenure (by A. R. K.) of an I.C.I. Fellowship.

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[17] Horning, Horning, and Platt, *J. Amer. Chem. Soc.*, 1948, **70**, 288.
[18] Billman and Rendall, *ibid.*, 1944, **66**, 540.

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32. *Purines, Pyrimidines, and Glyoxalines. Part VII.* New Syntheses of 2-Thiouracils and 2-Thiothymines.*

By G. SHAW and R. N. WARRENER.

β-Ethoxyacryloyl and β-methoxy-α-methylacryloyl *iso*thiocyanate have been prepared by reaction of the corresponding acid chlorides with potassium thiocyanate. The *iso*thiocyanates with ammonia and primary amines gave linear acylthioureas which when treated with dilute aqueous alkali afforded 1-substituted 2-thiouracils and 2-thiothymines. Reaction of the acyl *iso*thiocyanates with phenylhydrazine similarly gave acylthiosemicarbazides which with alkali afforded thiotriazoles.

IN Part III [1] of this series a new synthesis of 1-substituted 5-cyano-2-thiouracils, by the reaction of a primary amine with a 5-cyanothiazine, was described. As part of our anti-metabolite studies and for other reasons we also wished to prepare 1-substituted 2-thiouracils and 2-thiothymines by routes which would be suitable for the preparation of nucleosides

* Part VI, *J.*, 1957, 3207.

[1] Part III, Atkinson, Shaw, Schaffner, and Warrener, *J.*, 1956, 3847.

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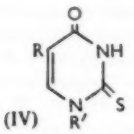
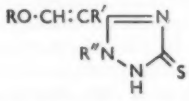
from amino-sugars. The only recorded formation of derivatives of this type appears to be due to Johnson and his co-workers who obtained 1-methyl-2-thiothymine [2] and 1-benzyl-2-thiouracil [3] as by-products from the acid hydrolysis of 1 : 5-dimethyl-2-ethylthio- and 1-benzyl-2-benzylthio-4-pyrimidone respectively; the major products in these reactions were the 2-pyrimidones. We now report a simple route to 2-thiopyrimidones.

Ethyl β-ethoxyacrylate, prepared by an improvement of Deno's method,[4] was hydrolysed to the acid (I; R = Et, R′ = H), the dried sodium salt of which with thionyl chloride gave an excellent yield of the acid chloride. With potassium thiocyanate in acetonitrile [5] at

RO·CH:CR′·CO_2H (I) RO·CH:CR′·CO·NCS (II) RO·CH:CR′·CO·NH·CS·NHR″ (III)



(IV)



(V)

room temperature this gave a good yield of the acyl *iso*thiocyanate (II; R = Et, R′ = H), which with ammonia, methylamine, aniline, and phenylhydrazine gave almost quantitatively the acylthioureas (III; R = Et, R′ = H; R″ = H, Me, Ph) and the thiosemicarbazide (III; R = Et, R′ = H, R″ = NHPh). Treatment of the thioureas with warm dilute sodium hydroxide solution readily gave the 2-thiouracils (IV; R = H, R′ = H, Me, Ph) but the thiosemicarbazide, not unexpectedly, was dehydrated by alkali to the thiotriazole (V; R = Et, R′ = H, R″ = Ph).

Addition of bromine to methyl α-methylacrylate and reaction of the resulting methyl αβ-dibromo-α-methylpropionate with hot methanolic sodium methoxide gave a mixture of methyl ββ-dimethoxy-α-methylpropionate and β-methoxy-α-methylacrylate which when distilled from sodium hydrogen sulphate gave an excellent yield of the last-mentioned ester; [6] alkaline hydrolysis then gave the acid (I; R = R′ = Me).[6] This was smoothly converted *via* the acid chloride into the *iso*thiocyanate (II; R = R′ = Me) which with ammonia, methylamine, aniline, and phenylhydrazine gave linear compounds (III; R = R′ = Me, R″ = H, Me, Ph, NHPh). The reaction of the compounds (III; R = R′ = Me, R″ = Me, Ph, NHPh) with sodium hydroxide solution gave excellent yields of the 2-thiothymines (IV; R = Me, R′ = Me, Ph) and the thiotriazole (V; R = R′ = Me, R″ = Ph). However the thiourea (III; R = R′ = Me, R″ = H) was recovered unchanged from warm dilute sodium hydroxide solution, and was decomposed by more drastic treatment. For the preparation of the 2-thiopyrimidones, isolation of the intermediate thioureas is not necessary. Thus the *iso*thiocyanate (II; R = R′ = Me) with an alkaline solution of glycine gave directly the substituted 2-thiothymine (IV; R = Me, R′ = CH_2·CO_2H).

Experimental

Thionyl chloride was purified before use by distillation from dry quinoline and fractionation of the distillate. Compounds were dried for analysis at 56°/0·1 mm. for 1—2 hr.

β-Ethoxyacryloyl Chloride (cf. ref. 4).—Ethyl bromoacetate (334 g.), ethyl orthoformate (400 ml.), and zinc shavings (1 kg.) gave ethyl β-ethoxyacrylate (104 g.), b. p. 189—191°; Deno [4] records b. p. 189—193°. The ester (48 g.) was stirred on a water-bath with 2N-sodium hydroxide (180 ml.) for 2 hr., cooled, and acidified, to precipitate β-ethoxyacrylic acid (35 g.), m. p. 109°; Tschitschibabin [4] gives m. p. 110·5°.

Dry sodium β-ethoxyacrylate (prepared from the acid by neutralisation with sodium

[2] Johnson and Clapp, *J. Biol. Chem.*, 1908, **5**, 56.
[3] Johnson and Joyce, *J. Amer. Chem. Soc.*, 1916, **38**, 1390.
[4] Deno, *J. Amer. Chem. Soc.*, 1947, **69**, 2233; Tschitschibabin, *J. prakt. Chem.*, 1906, **73**, 335.
[5] Cf. Elmore, Ogle, Fletcher, and Toseland, *J.*, 1956, 4458.
[6] Bieber, *Compt. rend.*, 1951, **233**, 655.

hydroxide solution and evaporation *in vacuo*) (15 g.) was refluxed with thionyl chloride (10 ml.) in ether (200 ml.) for 4 hr., kept overnight, and filtered through asbestos. Distillation of the filtrate *in vacuo* gave β-*ethoxyacryloyl chloride* (11·5 g.), b. p. 104°/35 mm. (Found: C, 44·45; H, 5·35. $C_5H_7O_2Cl$ requires C, 44·65; H, 5·25%).

β-*Ethoxyacryloyl* iso*Thiocyanate*.—The foregoing acid chloride (9·33 g.) in dry acetonitrile (50 ml.) was shaken with freshly dried potassium thiocyanate (6·8 g.) for 3 hr., then filtered from potassium chloride, and the orange filtrate distilled *in vacuo*, to give pale yellow β-*ethoxyacryloyl* iso*thiocyanate* (6·2 g.), b. p. 90°/1·5 mm. (Found: C, 46·45; H, 4·7; N, 8·85. $C_6H_7O_2NS$ requires C, 45·85; H, 4·5; N, 8·9%).

2-*Thiouracil*.—The foregoing *iso*thiocyanate (1·35 g.) reacted vigorously with 3·34N-methanolic ammonia (3 ml.). N-β-*Ethoxyacryloylthiourea* separated; it recrystallised from ethanol as prisms (0·74 g.), m. p. 165° (Found: C, 41·6; H, 5·85; N, 15·85. $C_6H_{10}O_2N_2S$ requires C, 41·4; H, 5·8; N, 16·1%). The thiourea (0·5 g.) was heated on a water-bath for 45 min. with 2N-sodium hydroxide (5 ml.), cooled, and acidified with hydrochloric acid, to precipitate a gummy solid. This, when triturated with a little ethanol, gave 2-thiouracil (0·05 g.) which separated from water as needles, m. p. 304° (decomp.) (Found: C, 37·45; H, 3·45; N, 21·5. Calc. for $C_4H_4ON_2S$: C, 37·5; H, 3·15; N, 21·85%).

1-*Methyl*-2-*thiouracil*.—The *iso*thiocyanate (0·84 g.) in ether (15 ml.) was treated with 33% methanolic methylamine (0·5 ml.). The solution was evaporated to dryness and the residue crystallised from ethanol, to give N-β-*ethoxyacryloyl*-N′-*methylthiourea* (0·45 g.) as needles, m. p. 124° (Found: C, 45·1; H, 6·35; N, 14·7. $C_7H_{12}O_2N_2S$ requires C, 44·7; H, 6·45; N, 14·9%). The thiourea (0·35 g.) was warmed for 10 min. with 2N-sodium hydroxide (4 ml.). The cooled solution when acidified gave a precipitate of 1-*methyl*-2-*thiouracil* (0·23 g.) which recrystallised from ethanol as needles, which changed to plates, m. p. 228° (Found: C, 42·55; H, 3·95; N, 19·6. $C_5H_6ON_2S$ requires C, 42·25; H, 4·25; N, 19·7%).

1-*Phenyl*-2-*thiouracil*.—The *iso*thiocyanate (1·15 g.) and aniline (0·7 g.) were mixed in ether (25 ml.). Precipitated N-β-*ethoxyacryloyl*-N′-*phenylthiourea* (1·25 g.) crystallised from ethanol as plates, m. p. 152° (Found: C, 57·7; H, 5·4; N, 11·0. $C_{12}H_{14}O_2N_2S$ requires C, 57·6; H, 5·65; N, 11·2%). This (0·85 g.) was heated on a water-bath with 2N-sodium hydroxide (5 ml.) for 15 min., a clear solution being obtained; this was acidified and the solid filtered off. 1-*Phenyl*-2-*thiouracil* (0·68 g.) crystallised from ethanol as laths, m. p. 236° (Found: C, 58·85; H, 3·85; N, 13·6. $C_{10}H_8ON_2S$ requires C, 58·8; H, 3·95; N, 13·7%).

5-β-*Ethoxyvinyl*-2 : 3-*dihydro*-1-*phenyl*-3-*thio*-1 : 2 : 4-*triazole*.—The *iso*thiocyanate (0·87 g.), phenylhydrazine (0·6 g.), and ethanol (5 ml.) gave a precipitate of N^1-β-*ethoxyacryloyl*-N^2-*phenylthiosemicarbazide* (0·87 g.), plates (from ethanol), m. p. 161° (Found: C, 54·05; H, 5·8; N, 15·6. $C_{12}H_{15}O_2N_3S$ requires C, 54·35; H, 5·7; N, 15·85%). The thiosemicarbazide (0·4 g.) was heated with 2N-sodium hydroxide (5 ml.) for 5 min. and the cooled solution acidified; the precipitated 5-β-*ethoxyvinyl*-2 : 3-*dihydro*-1-*phenyl*-3-*thio*-1 : 2 : 4-*triazole* (0·37 g.) separated from ethanol as prisms, m. p. 161° (Found: C, 58·3; H, 5·1; N, 16·8. $C_{12}H_{13}ON_3S$ requires C, 58·3; H, 5·3; N, 17·0%).

β-*Methoxy*-α-*methylacrylic Acid*.—The following method has been found to be suitable for the preparation of this acid, which was described without experimental directions by Bieber.[6]

Methyl αβ-dibromo-α-methylpropionate [6] (467 g.) in methanol (500 ml.) was added to a hot solution from sodium (82·6 g.) and methanol (1 l.) at a rate sufficient to keep the mixture boiling. Next morning the mixture was filtered from sodium bromide which was washed with methanol. The filtrate and washings were evaporated to about half volume and sodium bromide was again removed. Most of the solvent was removed, the semi-gelatinous residue treated with water (250 ml.), and the precipitated oil extracted into ether. The dried solution was evaporated and the residue heated with freshly fused sodium hydrogen sulphate (1·5 g.) at 170° under a small fractionating column until evolution of ethanol was complete. The residue, distilled *in vacuo*, gave methyl β-methoxy-α-methylacrylate (159 g., 68%), b. p. 66—67°/10 mm., n_D^{23} 1·455; Bieber gives n_D^{18} 1·460. The ester (39 g.) was heated on a water-bath with 2N-sodium hydroxide (255 ml.) with stirring until a clear solution was obtained (3 hr.); this was cooled and acidified with 2N-hydrochloric acid (225 ml.), to precipitate β-methoxy-α-methylacrylic acid (35·5 g.) which separated from light petroleum (b. p. 60—80°) as plates, m. p. 106° (Found: C, 51·85; H, 7·0. Calc. for $C_5H_8O_3$: C, 51·7; H, 6·95%).

β-*Methoxy*-α-*methylacryloyl Chloride*.—Sodium β-methoxy-α-methylacrylate was prepared by neutralising (to phenolphthalein) a suspension of the acid in water with 2N-sodium hydroxide.

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The solution was evaporated to dryness *in vacuo* and the residual salt dried at 100°/0·5 mm. for 4·5 hr. before use; almost exactly 1 mol. of water was lost during the drying. To a suspension of this salt (25·72 g.) in ether (100 ml.) was added thionyl chloride (16 ml.) in ether (100 ml.). When the initial vigorous reaction had subsided, the mixture was boiled under reflux for 3 hr., filtered, and evaporated to an oil which was distilled *in vacuo*, giving *β-methoxy-α-methylacryloyl chloride* (20·0 g.), b. p. 102°/35 mm. (Found: C, 45·2; H, 5·2. $C_5H_7O_2Cl$ requires C, 44·6; H, 5·25%). The acid chloride with a little water gave the acid, m. p. and mixed m. p. 105°.

β-Methoxy-α-methylacryloyl iso*Thiocyanate*.—To a solution of the foregoing acid chloride (8·6 g.) in dry acetonitrile (50 ml.) was added dry potassium thiocyanate (6·2 g.) giving, as in the analogous case, *β-methoxy-α-methylacryloyl* iso*thiocyanate* (7·2 g.), b. p. 102°/2 mm. (Found: C, 45·85; H, 4·2; N, 8·75. $C_6H_7O_2NS$ requires C, 45·85; H, 4·5; N, 8·9%). The *iso*thiocyanate crystallised at room temperature as large plates which melted a little above room temperature. The compound should be kept in the refrigerator, otherwise it slowly darkens and deposits some sludge.

1-*Methyl*-2-*thiothymine*.—25% Ethanolic methylamine (0·6 ml.) was added to a solution of this *iso*thiocyanate (0·86 g.) in methanol (5 ml.); a vigorous reaction occurred and a crystalline precipitate separated immediately; N-(*β-methoxy-α-methylacryloyl*)-N′-*methylthiourea* (0·55 g.) recrystallised from ethanol as thick needles, m. p. 140° (Found: C, 44·45; H, 6·15; N, 14·8. $C_7H_{12}O_2N_2S$ requires C, 44·7; H, 6·45; N, 14·9%). The thiourea (0·28 g.) was gently warmed with 2N-sodium hydroxide (2 ml.) until a clear solution was obtained. This was cooled and acidified to precipitate 1-methyl-2-thiothymine (0·19 g.) which separated from ethanol as needles, m. p. 226—227° (Johnson and Clapp [2] give m. p. 229—230°) (Found: C, 45·85; H, 4·9; N, 17·85. Calc. for $C_6H_8ON_2S$: C, 46·15; H, 5·15; N, 17·95%).

1-*Phenyl*-2-*thiothymine*.—The *iso*thiocyanate (0·5 g.) with aniline (0·5 g.) in ethanol (5 ml.) gave N-(*β-methoxy-α-methylacryloyl*)-N′-*phenylthiourea* (0·6 g.), needles (from ethanol), m. p. 110—112° (Found: C, 57·8; H, 5·4; N, 11·1. $C_{12}H_{14}O_2N_2S$ requires C, 57·6; H, 5·65; N, 11·2%). The thiourea (0·2 g.) dissolved after a few min. in 2N-sodium hydroxide; acidification of the cooled solution gave 1-*phenyl*-2-*thiothymine* (0·15 g.), needles (from ethanol), m. p. 202—203° (Found: C, 60·4; H, 4·75; N, 12·4. $C_{11}H_{10}ON_2S$ requires C, 60·55; H, 4·6; N, 12·85%).

1-*Carboxymethyl*-2-*thiothymine*.—The *iso*thiocyanate (1·12 g.) was shaken with glycine (0·54 g.) in 1·94N-sodium hydroxide (7·4 ml.) until a clear solution was obtained (10 min.) and then for a further 10—15 min., cooled, acidified, and kept at 0° overnight. A solid precipitate separated. This was dissolved in aqueous sodium hydrogen carbonate, the solution filtered, and the filtrate acidified to give 1-*carboxymethyl*-2-*thiothymine* (0·7 g.) which crystallised from water as needles, m. p. 246—247° (decomp.) (Found: C, 41·9; H, 3·8; N, 13·8. $C_7H_8O_3N_2S$ requires C, 42·0; H, 4·05; N, 14·0%).

2 : 3-*Dihydro*-5-(*β-methoxy-α-methylvinyl*)-1-*phenyl*-3-*thio*-1 : 2 : 4-*triazole*.—Phenylhydrazine (0·5 g.) in ethanol (5 ml.) was added to the *iso*thiocyanate (0·68 g.); the cooled solution afforded N^1-(*β-methoxy-α-methylacryloyl*)-N^3-*phenylthiosemicarbazide* (0·75 g.), plates (from ethanol), m. p. 180—181° (decomp.) (Found: C, 54·6; H, 5·6; N, 15·6. $C_{12}H_{15}O_2N_3S$ requires C, 54·35; H, 5·7; N, 15·85%). The thiosemicarbazide (0·31 g.) was warmed with 2N-sodium hydroxide until the solution was clear. Acidification of this precipitated 2 : 3-*dihydro*-5-(*β-methoxy-α-methylvinyl*)-1-*phenyl*-3-*thio*-1 : 2 : 4-*triazole* (0·28 g.) which crystallised from ethanol as needles, m. p. 195—196° (Found: C, 58·45; H, 5·45; N, 16·9. $C_{12}H_{13}ON_3S$ requires C, 58·3; H, 5·3; N, 17·0%).

N-*β-Methoxy-α-methylacryloylthiourea*.—The *iso*thiocyanate (0·935 g.) in a little ethanol was added to saturated methanolic ammonia (1·5 ml.), to precipitate N-*β-methoxy-α-methylacryloylthiourea* (0·85 g.) which crystallised from ethanol as prisms, m. p. 163° (Found: C, 41·15; H, 5·7; N, 16·0. $C_6H_{10}O_2N_2S$ requires C, 41·4; H, 5·8; N, 16·1%). The thiourea was recovered unchanged from its solution in 2N-sodium hydroxide; longer heating gave hydrogen sulphide and no evidence of pyrimidine formation.

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33. *Purines, Pyrimidines, and Glyoxalines. Part VIII.* New Syntheses of Uracils and Thymines.*

By G. Shaw and R. N. Warrener.

Uracils and thymines have been prepared by the reaction of β-ethoxyacryloyl and β-methoxy-α-methylacryloyl *iso*cyanate respectively with (*a*) ammonia or primary amines (followed by cyclisation of the resulting acylureas) and (*b*) ethanol (followed by reaction of the β-alkoxyacryloylurethanes so formed with primary amino-compounds). The *iso*cyanates were prepared from the acid chlorides and silver cyanate.

Part V [1] of this series described new syntheses of uracil and its 1-substituted derivatives by the reaction of ammonia or a primary amine with propioloylurethane or β-ethoxyacryloylurethane (IV; R = Et, R′ = H). However the preparation of these intermediates was not entirely satisfactory, so we examined alternatives. With a view to extending the reactions to syntheses of 1-substituted thymine derivatives, we studied first the β-alkoxyacryloylurethanes.

In an attempt to prepare the potential thymine precursor (IV; R = R′ = Me) by the reaction of β-methoxy-α-methylacryloyl chloride * (I; R = R′ = Me) with sodiourethane in benzene only the bisurethane derivative, $EtO_2C{\cdot}NH{\cdot}CH{:}CMe{\cdot}CO{\cdot}NH{\cdot}CO_2Et$, was isolated. When sodium β-methoxy-α-methylacrylate was treated with a half molar quantity of thionyl chloride and the product, presumably the anhydride, warmed with urethane, the urethane, $EtO_2C{\cdot}NH{\cdot}CH{:}CMe{\cdot}CO_2H$, was obtained, again by replacement of the methoxy-group.

In Part VII we described syntheses of thiouracils and thiothymines from β-alkoxyacryloyl *iso*thiocyanates and primary amines. We have extended this reaction to analogous oxy-compounds.

β-Methoxy-α-methylacryloyl chloride (I; R = R′ = Me) with silver cyanate in benzene at room temperature readily gave a crystalline compound which, though so reactive as to be unstable, was clearly the *iso*cyanate (IV; R = R′ = Me). In air it immediately gave a solid which rapidly evolved carbon dioxide, leaving a crystalline residue of the *NN*′-diacylurea. Benzoyl *iso*cyanate and water also give some dibenzoylurea although the major product in this case is benzamide.[2] It has been suggested that diacylureas are formed by reaction of excess of acyl *iso*cyanate with the amide first formed: $R{\cdot}CO{\cdot}NH_2 + R{\cdot}CO{\cdot}NCO \longrightarrow (R{\cdot}CO{\cdot}NH)_2CO$. It seems much more likely however that the reaction proceeds *via* a carbamic anhydride: $2R{\cdot}CO{\cdot}NCO + H_2O \longrightarrow (R{\cdot}CO{\cdot}NH{\cdot}CO)_2O \longrightarrow R{\cdot}CO{\cdot}N(CO_2H){\cdot}CO{\cdot}NH{\cdot}CO{\cdot}R \longrightarrow (R{\cdot}CO{\cdot}NH)_2CO + CO_2$.

The *iso*cyanate (II; R = R′ = Me) reacted violently with ammonia, methylamine, aniline, and phenylhydrazine, to give the linear derivatives (III; R = R′ = Me, R″ = H, Me, Ph, or Ph·NH respectively). The acylureas (III; R = R′ = Me, R″ = H, Me, or Ph) were converted into the corresponding thymines (V; R = Me, R′ = H, Me, or Ph) when warmed respectively with aqueous ammonia, methylamine, and sodium hydroxide. The last base with the acylureas (III; R = R′ = Me, R″ = H, Me) also gave a small yield of pyrimidines although reaction conditions were difficult to define and in one case this reaction gave a compound $C_{11}H_{18}O_6N_2$, which was a molecular complex of the urea (III; R = R′ = Me, R″ = H) and β-methoxy-α-methylacrylic acid, since it gave these compounds when sublimed *in vacuo*. The semicarbazide (III; R = R′ = Me, R″ = Ph·NH) when warmed with sodium hydroxide solution gave the triazole (VI; R = R′ = Me, R″ = Ph).

* Part VII, preceding paper.

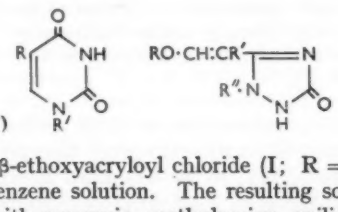
[1] Part V, Atkinson, Maguire, Ralph, Shaw, and Warrener, *J.*, 1957, 2363.
[2] Billeter, *Ber.*, 1903, **36**, 3218; Arcus and Prydal, *J.*, 1954, 4018.

XUM

The *iso*cyanate (II; R = R′ = Me) with ethanol gave the acylurethane (IV; R = R′ = Me) in excellent yield. This with ammonia, methylamine, and aniline readily afforded the thymines (V; R = Me, R′ = H, Me, Ph) respectively. An intermediate acylurea (III; R = R′ = Me, R″ = Ph) was obtained from the reaction of the urethane with aniline.

(I) RO·CH:CR′·COCl RO·CH:CR′·CO·NCO (II)

(III) RO·CH:CR′·CO·NH·CO·NHR″ RO·CH:CR′·CO·NH·CO_2Et (IV)



(V) (VI)

In a similar manner, β-ethoxyacryloyl chloride (I; R = Et, R′ = H) reacted readily with silver cyanate in benzene solution. The resulting solution of the acyl *iso*cyanate (II; R = Et, R′ = H) with ammonia, methylamine, aniline, and phenylhydrazine gave the linear derivatives (III; R = Et, R′ = H, R″ = H, Me, Ph, or Ph·NH respectively). The acylureas (III; R = Et, R′ = H, R″ = H, Me, or Ph) were cyclised to the corresponding uracils (V; R = H, R′ = H, Me, Ph) when treated with dilute alkali or sublimed *in vacuo*.

1-Methyluracil (V; R = H, R′ = Me) was also obtained directly by reaction of β-ethoxyacryloyl chloride with methylurea in boiling benzene containing a trace of sulphuric acid.

The last-mentioned *iso*cyanate with ethanol readily gave the acylurethane (IV; R = Et, R′ = H) which we prepared previously from ethyl β-ethoxyacrylate and sodiourethane.[1] The conversion of the urethane into uracil and its derivatives was also described in Part V;[1] however an intermediate linear derivative has now been obtained from the urethane and aniline and this proved to have the structure Ph·NH·CH:CH·CO·NH·CO_2Et where replacement of the β-alkoxy-group has occurred, as in reaction of the α-cyano-derivative (IV; R = Et, R′ = CN) with aniline[3] but differing from the reaction of the α-methyl compound (IV; R = R′ = Me) described above. It appears that, in compounds of type (IV), increasing nucleophilic character of the α-substituent decreases reactivity of the β-alkoxy-group (at least towards nucleophiles), corresponding to a decrease in the polarisation of the αβ-double bond.

Experimental

Compounds were dried (P_2O_5) for analysis at 56°/0·1—0·5 mm.

Reaction of β-Methoxy-α-methylacryloyl Chloride with Urethane.—A solution of urethane (4·65 g.) in dry ether (20 ml.) was boiled with a suspension of sodium powder (1·08 g.) in dry ether (100 ml.) for 10 hr., reaction then appearing to be complete. The resulting suspension of sodiourethane was treated with β-methoxy-α-methylacryloyl chloride (Part VII) (6·2 g.) in ether (20 ml.) and, after a vigorous reaction had subsided, the mixture was boiled for 3 hr., kept overnight, and filtered. The filtrate was evaporated to an oil which was distilled *in vacuo*. A viscous distillate was obtained with a wide boiling range (112—143°/0·5 mm.); this partly crystallised and, recrystallised from ethanol, gave *N-ethoxycarbonyl-β-(N-ethoxycarbonylamino)-α-methylacrylamide* (0·1 g.) as needles, m. p. 172—174° (Found: C, 49·25; H, 6·3; N, 11·65. $C_{10}H_{16}O_5N_2$ requires C, 49·2; H, 6·6; N, 11·45%).

β-(N-Ethoxycarbonylamino)-α-methylacrylic Acid.—Thionyl chloride (1·5 ml.) was shaken with a suspension of finely ground dry sodium β-methoxy-α-methylacrylate (5·1 g.) in dry ether (50 ml.) for 10 min., then kept overnight. The mixture was filtered, the filtrate was evaporated to an oil which was heated on a water-bath with urethane (1·9 g.) in ether (20 ml.) for 1 hr., and the resulting oil cooled. *β-(N-Ethoxycarbonylamino)-α-methylacrylic acid* (2·3 g.) separated and

[3] Shaw *J.*, 1955, 1834.

recrystallised from ethanol or ethyl acetate as needles, m. p. 193—194° (decomp.) (Found: C, 48·3; H, 6·55; N, 7·8. $C_7H_{11}O_4N$ requires C, 48·55; H, 6·4; N, 8·1%), soluble in solutions of sodium hydrogen carbonate or ammonia and recovered therefrom on acidification.

Reaction of β-Methoxy-α-methylacryloyl Chloride with Silver Cyanate.—Silver cyanate (dried *in vacuo* over P_2O_5 at 100°) (16 g.) was shaken with the acid chloride (10·5 g.) in benzene (50 ml.), heat being evolved. The whole was then boiled for 30 min. (alternatively shaken for 3 hr. at room temperature). The supernatant liquid was rapidly decanted from silver salts, and the latter were washed by stirring them with benzene and again decanting the liquor. The solvent was removed, and the residue distilled *in vacuo* with rigorous exclusion of moisture; β-*methoxy*-α-methylacryloyl *iso*cyanate (5·65 g.) boiled at 57°/0·5 mm., crystallised in ice, and remelted at about room temperature. The intense reactivity of this substance towards atmospheric moisture precluded its being weighed for analysis without special apparatus. For most purposes the benzene solution obtained above may be used directly.

NN′-*Di*-(β-*methoxy*-α-*methylacryloyl*)*urea*.—When the foregoing *iso*cyanate was exposed to air an immediate vigorous reaction occurred, giving a solid which rapidly liberated carbon dioxide to leave crystalline NN′-*di*-(β-*methoxy*-α-*methylacryloyl*)*urea* which separated from ethyl acetate or water as needles, m. p. 186° (Found: C, 51·5; H, 6·1; N, 11·15. $C_{11}H_{16}O_5N_2$ requires C, 51·55; H, 6·3; N, 10·95%).

N-*Ethoxycarbonyl*-β-*methoxy*-α-*methylacrylamide*.—A suspension of dry silver cyanate (12 g.) in benzene (50 ml.) containing β-methoxy-α-methylacryloyl chloride (6 g.) was boiled for 30 min., then treated with dry ethanol (5 ml.), cooled, and filtered. The filtrate was washed with aqueous sodium hydrogen carbonate and water, dried, and evaporated *in vacuo* to a syrup which crystallised when rubbed with light petroleum (b. p. 40—60°). N-*Ethoxycarbonyl*-β-*methoxy*-α-*methylacrylamide* (6 g.) separated from chloroform–light petroleum (b. p. 60—80°) as prisms, m. p. 103°, which partly sublimed when dried for analysis (Found: C, 51·55; H, 7·05; N, 7·55. $C_8H_{13}O_4N$ requires C, 51·35; H, 7·0; N, 7·5%).

Thymine.—(*a*) β-Methoxy-α-methylacryloyl *iso*cyanate and methanolic ammonia reacted violently. β-*Methoxy*-α-*methylacryloylurea* separated immediately; it recrystallised from ethanol as prisms, m. p. 147° (Found: C, 45·8; H, 6·1; N, 17·7. $C_6H_{10}O_3N_2$ requires C, 45·6; H, 6·4; N, 17·7%). The urea (0·25 g.) was heated on a water-bath with 15N-ammonia for 30 min. until the solvent had almost evaporated. The residue was treated with a little water, cooled, and acidified, affording thymine (0·1 g.), m. p. and mixed m. p. 310° (decomp.) (Found: C, 47·5; H, 4·95; N, 22·1. Calc. for $C_5H_6O_2N_2$: C, 47·6; H, 4·8; N, 22·2%). The urea (0·5 g.) soon dissolved in 2N-sodium hydroxide (5 ml.). After a few minutes the solution was acidified to give a precipitate of a *compound* (0·28 g.) which crystallised from water as needles, m. p. 122° (Found: C, 48·25; H, 6·5; N, 10·1. $C_{11}H_{18}O_6N_2$ requires C, 48·2; H, 6·6; N, 10·2%); when sublimed at 120°/0·1 mm. this gave two zones of crystalline material; the more volatile was β-methoxy-α-methylacrylic acid, m. p. and mixed m. p. 106°, and the second was β-methoxy-α-methylacryloylurea, m. p. and mixed m. p. 145°.

(*b*) *N*-Ethoxycarbonyl-β-methoxy-α-methylacrylamide (1 g.) was heated on a water-bath with 15N-ammonia (10 ml.) for 20 min.; crystals separated as the solution evaporated. The mixture was cooled and acidified with hydrochloric acid, and the precipitated thymine collected. This recrystallised from water as needles (0·28 g.), m. p. and mixed m. p. 308° (decomp.).

1-*Methylthymine*.—(*a*) *N*-Ethoxycarbonyl-β-methoxy-α-methylacrylamide (1 g.) was warmed with 25% aqueous methylamine (2 ml.) on a water-bath for 20 min. Crystals remained. These were dissolved in 2N-sodium hydroxide (3 ml.). Acidification precipitated 1-methylthymine (0·33 g.) which recrystallised from water as needles, m. p. 281° (Johnson and Clapp [4] give m. p. 280—282°) (Found: C, 51·6; H, 5·65; N, 20·0. Calc. for $C_6H_8O_2N_2$: C, 51·4; H, 5·75; N, 20·0%).

(*b*) β-Methoxy-α-methylacryloyl *iso*cyanate and an excess of methanolic methylamine gave a precipitate of N-(β-*methoxy*-α-*methylacryloyl*)-N′-*methylurea* which separated from ethanol as needles, m. p. 127° (Found: C, 48·95; H, 6·95; N, 16·45. $C_7H_{12}O_3N_2$ requires C, 48·85; H, 7·05; N, 16·25%). The urea (0·36 g.) was dissolved in 2N-sodium hydroxide (5 ml.); acidification precipitated unchanged urea (0·16 g.). The urea (0·25 g.) was warmed with aqueous methylamine (5 ml.) for 20 min. and the solution acidified and kept overnight, giving a precipitate of 1-methylthymine (0·08 g.), m. p. and mixed m. p. 280° (Found: C, 51·4; H, 5·55; N, 19·95%).

[4] Johnson and Clapp, *J. Biol. Chem.*, 1908, **5**, 56.

XUM

1-*Phenylthymine*.—(*a*) The foregoing *iso*cyanate was added to an ethereal solution of aniline. N-(β-*Methoxy*-α-*methylacryloyl*)-N′-*phenylurea*, which separated, formed needles, m. p. 144°, from ethanol (Found: C, 61·5; H, 5·95; N, 12·15. $C_{12}H_{14}O_3N_2$ requires C, 61·5; H, 6·00 N, 11·95%). The phenylurea (0·41 g.) was warmed with 2N-sodium hydroxide (5 ml.) with shaking until a clear solution was obtained. This was cooled and acidified, affording 1-*phenylthymine* (0·27 g.) which recrystallised from water as needles, m. p. 199° (Found: C, 65·25; H, 5·0; N, 13·9. $C_{11}H_{10}O_2N_2$ requires C, 65·35; H, 5·0; N, 13·85%). (*b*) *N*-Ethoxycarbonyl-β-methoxy-α-methylacrylamide (1 g.) and aniline (0·6 g.) were heated together on a water-bath for 1 hr., then kept overnight, and the residual oil treated with ether to precipitate *N*-(β-methoxy-α-methylacryloyl)-*N*′-phenylurea (0·2 g.), m. p. and mixed m. p. 143—144°, which with alkali gave 1-phenylthymine.

2 : 3-*Dihydro*-5-(β-*methoxy*-α-*methylvinyl*)-1-*phenyl*-1 : 2 : 4-*triazol*-3-*one*.—β-Methoxy-α-methylacryloyl *iso*cyanate when added to ethereal phenylhydrazine afforded a precipitate of N^1-(β-*methoxy*-α-*methylacryloyl*)-N^3-*phenylsemicarbazide* which separated from ethanol as prisms, m. p. 193° (Found: C, 57·95; H, 5·95; N, 16·95. $C_{12}H_{15}O_3N_3$ requires C, 57·8; H, 6·05; N, 16·85%). The semicarbazide (0·52 g.) was warmed with 2N-sodium hydroxide (10 ml.) with shaking until a clear red solution was obtained. Acidification precipitated a gum which solidified when rubbed with ethanol; the *triazolone* (0·42 g.) crystallised from ethanol as needles, m. p. 195—197° (Found: C, 62·55; H, 5·55; N, 18·45. $C_{12}H_{13}O_2N_3$ requires C, 62·3; H, 5·65; N, 18·15%).

Reaction of β-*Ethoxyacryloyl Chloride with Silver Cyanate*.—The acid chloride (10·2 g.) in benzene (50 ml.) was treated with silver cyanate (14 g.); the mixture became hot. It was shaken for 3 hr. and the supernatant solution used in the following reactions.

Uracil. The *iso*cyanate solution was added to an excess of ethereal ammonia: a violent reaction occurred, and a precipitate was formed. The mixture was evaporated to dryness and the residue of β-*ethoxyacryloylurea* crystallised from methanol as needles, m. p. 198° (Found: C, 45·7; H, 6·4; N, 17·6. $C_6H_{10}O_3N_2$ requires C, 45·55; H, 6·35; N, 17·7%). The urea (0·25 g.) was warmed with 2N-sodium hydroxide (4 ml.) for a few minutes to give a clear solution which was then acidified and continuously extracted with ethyl acetate for 3 hr. Evaporation of the solvent gave uracil (0·1 g.), m. p. and mixed m. p. 315°.

1-*Methyluracil*. (*a*) The *iso*cyanate solution was added to ethanolic methylamine, and the solution then evaporated *in vacuo* to give a crystalline residue; N-(β-*ethoxyacryloyl*)-N′-*methylurea* separated from ethanol as plates, m. p. 152° (Found: C, 49·0; H, 6·85; N, 16·1. $C_7H_{12}O_3N_2$ requires C, 48·85; H, 7·05; N, 16·25%). The methylurea (0·25 g.) was heated on a water-bath with aqueous methylamine (5 ml.). The residue was stirred with dilute hydrochloric acid and the precipitated 1-methyluracil (0·065 g.) collected; it had m. p. and mixed m. p. 229—230°. (*b*) A small quantity of the methylurea, sublimed at 150°/0·1 mm., gave a crystalline sublimate which separated from water and had m. p. 230°, not depressed by 1-methyluracil. (*c*) β-Ethoxyacryloyl chloride (1·1 g.) and methylurea were heated in benzene (50 ml.) containing a trace of sulphuric acid under reflux for 3 hr. The solution was decanted from a small residue, evaporated to a small volume, and cooled, to give a precipitate of 1-methyluracil (0·4 g.), m. p. and mixed m. p. 230°.

1-*Phenyluracil*. The *iso*cyanate solution was added to aniline in ether, and the resulting precipitate collected. N-β-*Ethoxyacryloyl*-N′-*phenylurea* crystallised from ethanol as plates, m. p. 183° (Found: C, 61·45; H, 6·0; N, 11·95. $C_{12}H_{14}O_3N_2$ requires C, 61·5; H, 6·0; N, 11·95%). The phenylurea (0·165 g.) was heated on a water bath with 2N-sodium hydroxide (3 ml.) and ethanol (3 ml.) for 1 hr. The cooled solution was acidified, affording a precipitate of 1-phenyluracil [1] (0·104 g.), m. p. and mixed m. p. 247°.

N^1-*Ethoxyacryloyl*-N^3-*phenylsemicarbazide*.—The *iso*cyanate solution was added to a solution of phenylhydrazine in ether; a precipitate of the *semicarbazide* was formed which recrystallised from ethanol as plates, m. p. 176—177° (Found: C, 57·95; H, 6·1; N, 16·4%).

β-*Ethoxy*-N-*ethoxycarbonylacrylamide*.—β-Ethoxyacryloyl chloride (3·6 g.) and silver cyanate (5 g.) were boiled in benzene (20 ml.) for 30 min. The cooled solution was treated with dry ethanol (4 ml.), then washed with sodium hydrogen carbonate solution and water, dried, and evaporated to an oil which crystallised when stirred with light petroleum. β-Ethoxy-*N*-ethoxycarbonylacrylamide [1] (1·8 g.) had m. p. and mixed m. p. 84°.

β-*Anilino*-N-*ethoxycarbonylacrylamide*.—The foregoing acrylamide (0·25 g.) and aniline (0·15 g.) were heated together on a water-bath for 1 hr. The cooled product crystallised under

ether. β-Anilino-*N*-ethoxycarbonylacrylamide [1] (0·15 g.) crystallised from light petroleum as prisms, m. p. and mixed m. p. 147°.

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34. *Kinetics of the Bromination of Some Aromatic Amines.*

By R. P. Bell and Eileen N. Ramsden.

Measurement of redox potentials has been used to follow the rate of bromination of *NN*-dialkylanilines in strongly acid solution, bromine concentrations in the range 10^{-3}—10^{-7}M being used. The observed rates decrease rapidly with increasing acid concentration, and by using the acidity functions of these solutions it is possible to evaluate second-order velocity constants for the reaction between bromine and the amine molecules: these lie in the range 10^{6}—10^{10} l. mole^{-1} sec.$^{-1}$. In some instances complications arise from complex formation between bromine and the amine cations.

Aromatic amines react very rapidly with aqueous bromine, and no reliable measurements have been made on the kinetics of this reaction. Francis [1] reported values for the relative rates of bromination of various anilines and phenols, based on competition experiments, but no attempt was made to control the acidity of the reaction mixture. Since it would be expected (and is borne out by our results) that an anilinium ion will react very much more slowly than an aniline molecule, little meaning can be attached even to his relative rates. Robertson and his co-workers [2] assessed the activity effect of the dimethylamino-group on the benzene ring at 5×10^{18}, a strongly deactivating group being used to obtain rates slow enough to be measured, but they give few kinetic results.

The present paper describes measurements of the rate of bromination of some *NN*-dialkylanilines. The second-order velocity constants obtained were in the range 10^{+6}—10^{+10} l. mole^{-1} sec.$^{-1}$, and two devices were used to obtain measurable rates. In the first place bromination was studied in concentrated aqueous acids (mostly 1—8M-sulphuric acid) in which only one part in 10^{5}—10^{10} of the amine is present as the reactive undissociated species. By adjusting the acid concentration, convenient rates can be obtained with a wide range of amines. In the second place the disappearance of bromine was followed by observing the redox potential of the solution, thus making it possible to use low initial concentrations and to follow a rapid change of bromine concentration through several powers of ten (normally in the range 10^{-3}—10^{-7}M).

Experimental

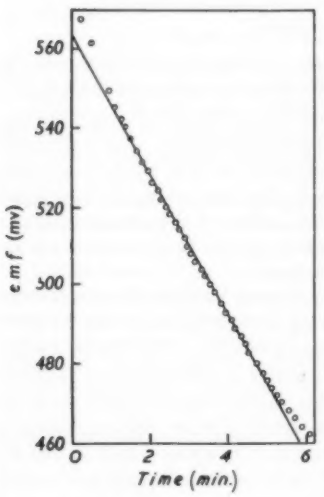
The amines were B.D.H. products, redistilled before use. All the inorganic reagents were of AnalaR grade, and the concentration of the acid solutions was checked by titration with standard alkali. Reactions were carried out at 25° ± 0·01° in a 150-c.c. beaker closed by a rubber stopper and fitted with a stirrer rotating at 1500 r.p.m. The beaker contained amine dissolved in acid, together with some potassium bromide, and the reaction was started by breaking a bulb containing 1 c.c. of a bromide–bromate solution. The bromide concentration was the same in the two solutions, and the usual initial concentrations were $[Br_2] = 0{\cdot}003$M, [amine] = 0·005—0·03M. In the strongly acid conditions used in our experiments the formation of bromine from bromate is almost instantaneous,[3] and identical results were obtained if the bulb contained bromine water or chloramine-T in place of bromate. Blank experiments

[1] Francis, *J. Amer. Chem. Soc.*, 1925, **47**, 2340.
[2] Robertson, de la Mare, and Swedlund, *J.*, 1953, 782.
[3] See "Tables of Chemical Kinetics," N.B.S. Circular 510, 1951, p. 669.

showed that loss of bromine by evaporation is negligible during the short times involved, and the results were not affected by the exclusion of light.

The redox potential of the solution was followed by a platinum gauze electrode, which was periodically cleaned by heating it in concentrated nitric acid. Ideally the comparison electrode should be chosen so as to avoid a liquid junction and various forms of silver–silver bromide and mercury–mercurous bromide electrodes were tried. However, these were not sufficiently stable under our conditions of high acidity and violent stirring, and the final measurements were made with a calomel half-cell having a side-arm dipping in the reaction solution and drawn to a fine point. This gave stable potentials during the duration of an experiment (2—30 min.), and the uncertain junction potential is no disadvantage since we are concerned only with the change in e.m.f. and not with its absolute value. The e.m.f. was measured by a Tinsley potentiometer, and all leads had earthed shields.

The Figure shows the course of a typical experiment. After an initial curved portion the e.m.f. varies linearly with time over a range of 60 mv, corresponding to a hundredfold variation in the bromine concentration. The concentration of bromide is effectively constant during each reaction, so that the e.m.f. is given by $E = E_0 + \frac{RT}{2F} \ln \frac{[Br_2]}{[Br^-]^2} = E_0^1 + 0{\cdot}0295 \log [Br_2]$: hence the linearity of the plot of E against t shows that the reaction is kinetically of the first order with respect to bromine. The initial curvature of this plot corresponds to a decrease in the amine concentration, but since 90% of the initial bromine has disappeared when the initial e.m.f. has fallen by 30 mv, the amine concentration is effectively constant beyond this point. Finally, when the bromine concentration has fallen below about 10^{-6}—10^{-7}M the e.m.f. begins to change more slowly, and eventually becomes constant. This is no doubt because the bromine concentration is no longer sufficient to poison the electrode, whose potential will begin to be controlled by some other system, for example the organic redox system represented by $RH + Br^- \rightleftharpoons RBr + H^+ + 2e$. Other possibilities are that dissolved oxygen is affecting the potential, or that there is an oxide layer on the platinum causing it to behave as a hydrogen-ion electrode. The point at which the linearity ceased varied from one experiment to another, and was not always reproduced on repeating an experiment: however, a linear portion corresponding to a variation of several powers of ten in bromine concentration was almost always present, and its failure to appear indicated that the electrode needed cleaning.



The analytical concentration of bromine in the solution can be written as $[Br_2]_a = [Br_2] + [Br_3^-] = [Br_2]\{1 + K[Br^-]\}$, where the equilibrium constant $K = 17{\cdot}8$ at 25°.[4] In a given experiment we can define an observed first-order velocity constant k_1 by

$$k_1 = \mathrm{d} \ln [Br_2]_a/\mathrm{d}t = \mathrm{d} \ln [Br_2]/\mathrm{d}t = 0{\cdot}0782 \ \mathrm{d}E/\mathrm{d}t \quad . \quad . \quad . \quad . \quad . \quad (1)$$

with E in mv. For a given amine k_1 will depend on the amine concentration c, the acidity of the medium, and the bromide concentration. Dependence on the two last factors will be controlled by the relative reactivities of the various species present, but *ceteris paribus* k_1 should be directly proportional to c. If n molecules of bromine react with one of amine, the value of c appropriate to the linear portion of the E against t curve is $c_0 - \frac{1}{n}[Br_2]_a^0$, c_0 and $[Br_2]_a^0$ representing initial concentrations. For all the reactions studied here $n = 1$. This was established by isolating the monobromo-derivatives (with the bromine atom *para* to the amino-group) in larger-scale experiments, and also by kinetic experiments in which one molecule of bromine was first allowed to react: when a second molecule of bromine was added the e.m.f.

[4] Griffith, McKeown, and Winn, *Trans. Faraday Soc.*, 1932, **28**, 101.

did not change faster than could be accounted for by evaporation. Plots of k_1 against $c_0 - [Br_2]_a{}^0$ were in fact linear, and the slope of these plots was used to obtain an apparent second-order constant $k_2{}^*$, defined by

$$k_2{}^* = \frac{k_1}{c} = \frac{0{\cdot}0782\ dE/dt}{c_0 - [Br_2]_a{}^0} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

The observed values of $k_2{}^*$ are tabulated in the following sections.

Our interpretation of the kinetic measurements depends on the assumption that the equilibria $Br_3^- \rightleftharpoons Br_2 + Br^-$ and $AH^+ + H_2O \rightleftharpoons A + H_3O^+$ (A = amine) are re-established rapidly compared with the bromination reactions being studied. While there is no direct evidence to support this assumption, it seems extremely probable. Both of these reactions are endothermic, but only to the extent of a few kcal./mole, and it is unlikely that their activation energies exceed this value.

In addition to the kinetic measurements, optical measurements were made in order to study the initial interaction between bromine and the amine solutions. These were carried out at room temperature, a Unicam spectrophotometer model S.P. 500 being used with 1-cm. quartz cells.

Results

Complex Formation between Bromine and Amines.—This subject will be dealt with here only in so far as it represents a complicating factor in the kinetic measurements, and a fuller study will be reported later. In an attempt to study spectrophotometrically the slow reaction between bromine and *p*-bromo-*NN*-dimethylaniline in 0·5M-sulphuric acid, it was found that the usual bromine peak at 3950 Å was gradually replaced by one at 4650 Å, which then slowly disappeared as bromination progressed. This suggests that most of the bromine reacts with amine to form a complex, with the result that the normal bromination reaction is greatly retarded. The effect is diminished by an increase of bromide concentration, but is almost independent of acid concentration in the range 0·5—6M-sulphuric acid, suggesting that the amine cation is involved. There are many examples of the formation of solid addition complexes between bromine and aromatic amines, *e.g.*, by pyridine and quinoline, respectively[5] $(C_5H_5N)_2HBr,Br_4$ and C_7H_7N,Br_4. Higher concentrations of *p*-bromo-*NN*-dimethylaniline and bromine produced a red precipitate which decomposed without melting at 85° and contained two molecules of bromine per molecule of amine. It liberated iodine from potassium iodide, and reacted with sodium hydrogen sulphite to re-form the original amine. It is interesting to note that the absorption spectrum of aqueous bromine is not modified by acid solutions of pyridine, quinoline, tetramethylammonium bromide, or trimethylphenylammonium bromide, although all these substances form solid addition compounds with bromine.

We shall not discuss here the probable structures of these complexes, as solids or in solution, but shall summarise briefly the results of spectrophotometric observations on various amine solutions immediately after adding 0·003M-bromine. The bromide concentration was 0·025M throughout, and the medium 6M-sulphuric acid. The *NN*-dialkyltoluidines gave no evidence of complex formation at amine concentrations of 0·01M, though they did so at 0·1M. *NN*-Dimethylaniline exhibited some complex formation even at 0·01M, but this disappeared as soon as the amine concentration had been reduced considerably by the normal bromination reaction. *NN*-Diethylaniline showed a strong peak attributable to complex formation, and this disappeared very slowly even with more dilute amine solutions: for this reason it has not proved possible to obtain a reliable value for the rate of bromination of this compound. The very slow rate observed either potentiometrically or spectrophotometrically may be due to the low concentration of free bromine present, or it may represent a slow reaction between the complex and an amine molecule. In any event it cannot be compared directly with the rates observed with the other amines which, on the above evidence, should not be materially affected by complex formation.

Measurements were also made to compare the absorption spectrum of bromine in water and in 6M-sulphuric acid: no difference was found. Similar experiments in hydrochloric acid gave evidence of the equilibrium $Br_2 + Cl^- \rightleftharpoons Br_2Cl^-$, with an equilibrium constant of about 0·6, which is less than the value 1·4 derived from partition measurements.[6] Most of the kinetic

[5] Grimaux, *Bull. Soc. chim. France*, 1882, **38**, 124.
[6] Dancaster, *J.*, 1924, 2039; Ray and Sarkar, *J.*, 1922, 1453.

experiments were therefore carried out in sulphuric acid to avoid complications due to formation of halide complex. The equilibrium $Br_2 + Br^- \rightleftharpoons Br_3^-$ was also studied spectrophotometrically in 6M-sulphuric acid, giving an equilibrium constant of about 13. This is appreciably lower than 17·8, the value for dilute aqueous solutions, but since we have no information about its variation with acid concentration we have preferred to use $K = 17{\cdot}8$ in the subsequent discussion.

Kinetic Results.—Most of the kinetic experiments were done with a bromide concentration of either 0·025M or 0·5M, and a range of acid concentrations. At each acid concentration several amine concentrations in the range 0·005—0·03M were usually investigated, but when complex

TABLE 1. *Bromination in sulphuric acid solution.*

a = acid concentration, moles/l. of solution. k_2^* = apparent second-order velocity constant, . mole^{-1} sec.$^{-1}$ (cf. eqn. 2). *A*, $[Br^-] = 0{\cdot}025$; *B*, $[Br^-] = 0{\cdot}5$.

NN-*Dimethylaniline*

	A						*B*					
a	4·96	5·73	5·94	6·24	6·31	6·76	4·88	5·44	6·09	6·09	7·13	
$-H_0$	2·11	2·47	2·57	2·74	2·78	3·02	2·08	2·33	2·66	2·66	3·22	
k_2^*	30·9	11·6	9·12	5·32	2·57	2·22	16·8	6·83	2·32	2·76	0·48	

NN-*Dimethyl*-o-*toluidine*

	A				*B*			
a	1·45	1·96	2·55	3·07	1·04	1·40	1·40	2·10
$-H_0$	0·37	0·66	0·99	1·24	0·13	0·35	0·35	0·76
k_2^*	3·16	2·76	1·18	0·66	3·77	2·15	2·61	0·82

NN-*Dimethyl*-m-*toluidine*

	A				*B*					
a	6·25	6·69	7·07	8·35	5·53	5·90	6·27	6·53	6·53	6·91
$-H_0$	2·74	2·99	3·20	3·90	2·38	2·55	2·76	2·90	2·90	3·12
k_2^*	6·59	3·42	2·82	0·32	13·7	7·50	3·20	3·11	3·36	1·69

NN-*Dimethyl*-p-*toluidine*

	A				*B*			
a	4·89	5·64	6·30	6·30	4·03	4·89	5·92	6·70
$-H_0$	2·08	2·44	2·77	2·77	1·67	2·08	2·57	2·99
k_2^*	6·57	2·48	0·77	0·85	20·4	4·13	0·76	0·12

NN-*Diethyl*-o-*toluidine*

	A					*B*		
a	0·255	0·510	1·05	1·44	1·99	1·03	1·51	1·88
$-H_0$	−0·56	−0·23	0·13	0·37	0·69	0·12	0·41	0·63
k_2^*	0·821	0·361	0·102	0·056	0·023	0·073	0·035	0·020

NN-*Diethyl*-m-*toluidine*

	A						*B*			
a	2·56	3·11	3·95	3·95	4·89	5·72	1·91	1·91	3·12	4·89
$-H_0$	0·99	1·24	1·61	1·61	2·09	2·47	0·64	0·64	1·44	2·09
k_2^*	110	35·2	8·75	10·6	2·13	0·59	89·8	87·0	14·3	1·04

NN-*Diethyl*-p-*toluidine*

	A			*B*			
a	3·05	3·55	3·95	1·82	2·26	2·77	3·16
$-H_0$	1·22	1·44	1·64	0·59	0·84	1·09	1·30
k_2^*	6·58	3·36	1·78	18·7	6·50	4·07	2·45

formation was suspected only concentrations below 0·01M were used, and in a few instances the velocity constant is based on experiments at 0·01M only. The initial bromine concentration was normally 0·003M. The results for sulphuric acid solutions are given in Table 1, the values of the acidity function H_0 being interpolated from the results of Hammett and Paul.[7]

[7] Hammett and Paul, *J. Amer. Chem. Soc.*, 1934, **56**, 827.

Discussion

All the results in Table 1 show that the reaction velocity decreases sharply with increasing acidity, as would be expected if the only reacting species were the amine molecule. Since the amines were present mainly as cations in all the solutions used, this implies on the simplest view that for a given amine and bromide concentration a plot of $\log_{10} k_2^*$ against H_0 should give a straight line of unit slope. These plots are all approximately linear, but their slopes are appreciably greater than unity, the average value being 1·20.

Slopes of greater than unity have been frequently found in logarithmic correlations between acidity functions and the rates of acid-catalysed reactions,[8] and have been reasonably attributed to the limitations of the arguments on which such correlations are based, notably the differences in chemical type between the reacting molecule and the indicators used in measuring the acidity functions. However, this explanation cannot apply here, since both the kinetic work and the measurements of acidity functions involve aromatic amines. Moreover, in the bromination reactions the acidity is not directly concerned in the reaction kinetics, but serves to reduce the concentration of reactive species by way of a pre-equilibrium so that a slope of unity seems particularly likely. A tertiary amine has not so far been used for measuring H_0, but measurements in this laboratory [9] with *NN*-dimethyl-2 : 4-dinitroaniline in sulphuric acid between 2M and 5M gave acidities parallel with those obtained by using *o*-nitroaniline or 4-chloro-2-nitroaniline: thus the usual acidity functions should apply to the tertiary amines used in our experiments.

If it is assumed that the concentration of undissociated amine is in fact inversely proportional to h_0 ($H_0 = -\log h_0$), then the exponent of 1·2 can only be attributed to a medium effect on the velocity constant of the bromination reaction. This interpretation is quite reasonable in view of the high concentrations of acid involved, and is confirmed by kinetic experiments in solutions of perchloric and phosphoric acids, where the medium effect is likely to be different. The rates in these solutions were in fact 25—100% higher than in sulphuric acid of the same acidity, the actual value depending upon the acid concentration and the nature of the amine.

In using our kinetic data as a direct measure of the reactivity of the amines it is necessary to assume that the amine cations are not brominated at an appreciable rate. Bromination experiments with trimethylphenylammonium bromide showed a rate of disappearance of bromine not significantly greater than the loss by evaporation in a blank experiment. Although the concentration of cations in our experiments is of the order of 10^6 greater than that of the undissociated amine, it would be surprising if it made a measurable contribution to the bromination rate. Robertson [2] has estimated the activating effect of the dimethylamino-group in the benzene ring as 5×10^{18}, and in the dimethylphenylammonium ion this activating effect is replaced by a powerful deactivation. It may be noted that any measurable bromination of cations would decrease the slopes of the plots of $\log k_2^*$ against H_0, and could not account for the observed slopes of greater than unity.

To obtain comparable values for the reactivities of the different amines we have used values of k_2^* at $H_0 = -1{\cdot}43$ (3·5M-sulphuric acid) interpolated or extrapolated from the data in Table 1, a slope of 1·20 being used throughout for the plot of $\log k_2^*$ against H_0. These values, $(k_2^*)_{1\cdot43}$, are given in the second and the third column of Table 2. The second-order velocity constants k_2 for the bromination of the amine in 3·5M-sulphuric acid are then given by the relation $\log k_2 = \log (k_2^*)_{1\cdot43} + pK_a + 1{\cdot}43$, where pK_a refers to the acid dissociation of the amine cation. These velocity constants are given in the last

[8] *E.g.*, Bell and Brown, *J.*, 1954, 774; Bell, Bascombe, and McCoubrey, *J.*, 1956, 1286; Gold and Hilton, *J.*, 1955, 843; Gold and Satchell, *J.*, 1955, 2622; 1956, 1635; Long and McIntyre, *J. Amer. Chem. Soc.*, 1954, **76**, 3240.

[9] Bell and Bascombe, to be published.

two columns of Table 2. The pK_a values are taken from the work of Hall and Sprinkle,[10] except that for *NN*-diethyl-*m*-toluidine, which was determined by measuring the optical density of the base in acid solution, in alkaline solution, and in phosphate buffer solutions

TABLE 2.

Amine	pK_a	log $(k_2^*)_{1\cdot 43}$		log k_2	
	[Br^-] =	0·025	0·5	0·025	0·05
NN-Dimethylaniline	5·06	2·29	1·95	8·84	8·50
NN-Dimethyl-*o*-toluidine	5·86	−0·50	−0·96	6·87	6·39
NN-Dimethyl-*m*-toluidine	5·24	2·48	2·29	9·21	9·02
NN-Dimethyl-*p*-toluidine	5·50	1·56	1·31	8·55	8·30
NN-Diethyl-*o*-toluidine	7·18	−2·54	−2·69	6·13	5·98
NN-Diethyl-*m*-toluidine	7·12	1·19	1·02	9·80	9·63
NN-Diethyl-*p*-toluidine	7·09	0·56	0·24	9·12	8·80

of pH 6·47, 6·81, and 7·17. The measurements were made with a Unicam S.P. 500 spectrophotometer, at 2550 Å, which corresponds to a peak in the absorption curve of the undissociated amine.

The velocity constants k_2 in Table 2 refer to the total bromine in the solution, which is present almost exclusively as Br_2 or Br_3^-. The concentrations of HOBr (a less active brominating agent) are very small, and it can easily be shown that H_2OBr^+ cannot be present in kinetically significant amounts. If k_2' and k_2'' are the second-order velocity constants for the reaction of Br_2 and Br_3^- with the amine, then k_2 is given by

$$k_2 = (k_2' + k_2''K[Br^-])/(1 + K[Br^-]) \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

where $K = [Br_3^-]/[Br_2][Br^-] = 17{\cdot}8$. It should be possible to test this equation by measurements over a wide range of bromide concentrations. However, as shown by Table 2, the effect of bromide concentration is not large, and extensive and accurate measurements would be required: moreover, the interpretation would be complicated by salt effects, uncertainty as to the value of K in the sulphuric acid media, and also the possibility of small effects due to formation of complex between bromine and the amine. We have therefore confined ourselves to measurements at the two bromide concentrations 0·025M and 0·5M, and Table 2 shows that the ratio of the velocities in these two solutions has the average value 1·8 : 1. Inserting this in eqn. 3 gives $k_2'/k_2'' \simeq 3$: this is similar to the ratios found by Bell and Spiro [11] for the reaction of Br_2 and Br_3^- with the enol and the anion of ethyl malonate. In our experiments in 0·025M-bromide, k_2 will be about 80% of k_2', and these values of k_2 are thus a good measure of both the absolute and the relative rates of reaction between Br_2 and the amine molecules.

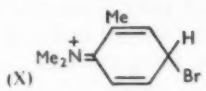
The values of k_2 are all in the range 10^6—10^{10} l. mole^{-1} sec.$^{-1}$ and thus represent extremely rapid reactions. By comparison with the rate of bromination of aromatic hydrocarbons [12] we can assess the activating power of the diethylamino- and dimethylamino-groups on the aromatic ring as about 10^{16}—10^{17}, though the comparison is not strictly valid, since the measurements refer to different solvents. This figure may be compared with 5×10^{18} estimated by Robertson [2] indirectly.

Several of the velocity constants in Table 2 are close to the values which would be expected in a collision reaction having zero activation energy. Solution reactions in this class would normally be regarded as diffusion-controlled, since the reaction rate is high enough to disturb the random spatial distribution of the reactants. However, these considerations do not apply here, since the reacting amine molecules are in dynamic equilibrium with a much larger concentration of amine cations, and the normal distribution of collisions will not be appreciably disturbed by the reaction.

NN-Dimethyl-*m*-toluidine reacts about twice as fast as *NN*-dimethylaniline, which

[10] Hall and Sprinkle, *J. Amer. Chem. Soc.*, 1932, **54**, 3469.
[11] Bell and Spiro, *J.*, 1953, 429.
[12] Data collected by Robertson *et al.*, ref. 2.

may be attributed to the presence of a methyl group *ortho* to the point of substitution. In *NN*-dimethyl-*p*-toluidine the methyl group blocks the normal point of attack, and the lower velocity refers to substitution in the less reactive *ortho*-position, weakly activated by the methyl group. *NN*-Dimethyl-*o*-toluidine reacts about 100 times more slowly than the other dimethylanilines: this is presumably because the methyl group hinders the attainment of a planar configuration in a transition state such as (X). The same effect is apparent, though to a smaller extent, in the higher pK_a value of dimethyl-*o*-toluidine, where steric hindrance will diminish the resonance stabilisation of the amine molecule.



(X)

NN-Diethyl-*m*-toluidine and *NN*-diethyl-*p*-toluidine are more reactive than the corresponding dimethyl-compounds, though the differences are not so great as in the pK_a values. On the other hand, *NN*-diethyl-*o*-toluidine reacts about four times more slowly than the dimethyl-compound, presumably because of the greater steric effect of the ethyl groups.

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PHYSICAL CHEMISTRY LABORATORY, OXFORD. [*Received, August 7th*, 1957.]

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35. *The Action of the Phenyl Radical on Anthracene and meso-Substituted Anthracenes.*

By R. O. C. NORMAN and WILLIAM A. WATERS.

Phenyl radicals can be prepared conveniently by the action of zinc powder on benzenediazonium salts suspended in acetone. These radicals can be substituted into anthracene in the *meso*-positions, but isolation of 9 : 9′ : 10 : 10′-tetrahydro-10 : 10′-diphenyl-9 : 9′-dianthryl indicates that the substitution occurs *via* phenyl-radical addition. 9-Methylanthracene reacts with phenyl radicals to give 9-methyl-10-phenylanthracene and not dianthrylethane. Both 9-methyl- and 9-phenyl-anthracene are more reactive towards phenyl radicals than is anthracene, but 9 : 10-dimethylanthracene is not reactive.

WHILST reactions between free phenyl radicals and organic liquids have been studied extensively, little attention has as yet been paid to reactions with solid organic compounds because of the difficulty of obtaining phenyl radicals uncontaminated with others in high enough concentration in organic solvents. Benzoyl peroxide produces phenyl radicals from benzoate radicals by the decomposition $Ph{\cdot}CO{\cdot}O{\cdot} \longrightarrow Ph{\cdot} + CO_2$, and reactive solutes, such as anthracene, interact with the benzoate radicals before this decomposition has taken place.[1] Tracer studies of reactions with olefins [2] have elaborated this fact. Other sources of phenyl radicals used by Hey and his colleagues [3-5] also give rise to radicals of two different types and are limited in their applicability. The decomposition of phenylmagnesium bromide in the presence of a cobaltous salt,[6] though it yields only phenyl radicals, is of little value because these radicals are so largely removed by interaction with the ether that is the necessary solvent,[7] that only small yields from interactions with added solutes are obtainable.

To surmount these difficulties we have examined the wider applicability of the reaction

[1] Roitt and Waters, *J.*, 1952, 2695.
[2] Bevington, *Proc. Roy. Soc.*, 1957, *A*, **239**, 420.
[3] Hey, Nechvatal, and Robinson, *J.*, 1951, 2892.
[4] Hey, Stirling, and Williams, *J.*, 1954, 2747.
[5] *Idem*, *J.*, 1955, 3963.
[6] Kharasch and Fields, *J. Amer. Chem. Soc.*, 1941, **63**, 2316.
[7] Norman and Waters, *J.*, 1957, 950.

between benzenediazonium salts and zinc powder in neutral acetone suspension, previously used by one of us for the phenylation of naphthalene,[8] and later for the rapid synthesis of triphenylarsine.[9] This reaction, which gives only phenyl radicals, can be conveniently carried out with the easily prepared solid benzenediazonium zincichloride, $(PhN_2)_2ZnCl_4$, or with the less reactive solid benzenediazonium fluoroborate. Though there is considerable interaction of phenyl radicals with acetone, this liquid is such a good solvent that high concentrations of solutes can be used, particularly since the reaction, being exothermic, mainly occurs at the boiling point.

Dr. J. I. G. Cadogan has informed us that in a similar reaction in which copper powder is used instead of zinc, the isomer ratios for the *p*-bromophenylation of nitrobenzene in nitrobenzene–acetone by the reactions

$$p\text{-}Br{\cdot}C_6H_4N_2BF_4 \xrightarrow{Cu} BrC_6H_4{\cdot}; \qquad BrC_6H_4{\cdot} + PhNO_2; \qquad p\text{-}BrC_6H_4{\cdot}NO_2\ (o, m, p)$$

are identical with those obtained by using *p*-bromobenzoyl peroxide [5]*, consequently the liberation of free phenyl radicals by the reduction of diazonium salts by metals in acetone suspension cannot be questioned.

We ourselves have used only zinc powder as the reducing agent and have studied thereby the reaction of phenyl radicals with anthracene and *meso*-substituted anthracenes. From anthracene, 9 : 10-diphenylanthracene and 9 : 9′ : 10 : 10′-tetrahydro-10 : 10′-diphenyl-9 : 9′-dianthryl (I) were obtained in 11 and 12% yield, respectively.

Whereas both methyl [10] and benzyl [11] radicals react with anthracene at moderate temperatures to give *meso*-radical adducts, *e.g.* 9 : 10-dibenzyl-9 : 10-dihydroanthracene, in higher yields than *meso*-substitution products, yet in the reaction with phenyl radicals no 9 : 10-dihydro-9 : 10-diphenylanthracene appears to be formed. However, isolation of the coupled dimer (I) indicates that the *meso*-phenylation of anthracene must follow the same additive mechanism as that already described for homolytic alkylation.[10,11] Evidently, phenyl radicals are much more effective than alkyl radicals in abstracting nuclear hydrogen atoms when necessary to regenerate a wholly aromatic system. 9 : 10-Dihydro-9 : 10-diphenylanthracene was not dehydrogenated by phenyl radicals under these conditions, so that of the two possible paths (*A*) and (*B*) for the phenylation process, (*B*) is the correct one; failure to isolate 9-phenylanthracene from the phenylation of anthracene is presumably due to 9-phenylanthracene's being much more reactive towards phenyl radicals than is anthracene (see below).

Another difference in reactivity between phenyl and methyl radicals is well examplified by the reaction of phenyl radicals with 9-methylanthracene. Nuclear attack at the *meso*-position seems to occur exclusively to give 9-methyl-10-phenylanthracene, whereas methyl radicals give only 1 : 2-di-9′-anthrylethane.[10] Phenylation gave neither 1 : 2-di-9′-anthrylethane nor 1 : 2-di-(10-phenyl-9-anthryl)ethane.

These latter observations are relevant to consideration of the mechanism of homolytic substitution of benzene derivatives, for the fact that phenyl radicals attack toluene to give mainly methyldiphenyls [12,13] whereas methyl radicals attack the side-chain to give benzyl radicals [11] exactly parallels these observations of phenyl and methyl radical attack on 9-methylanthracene.

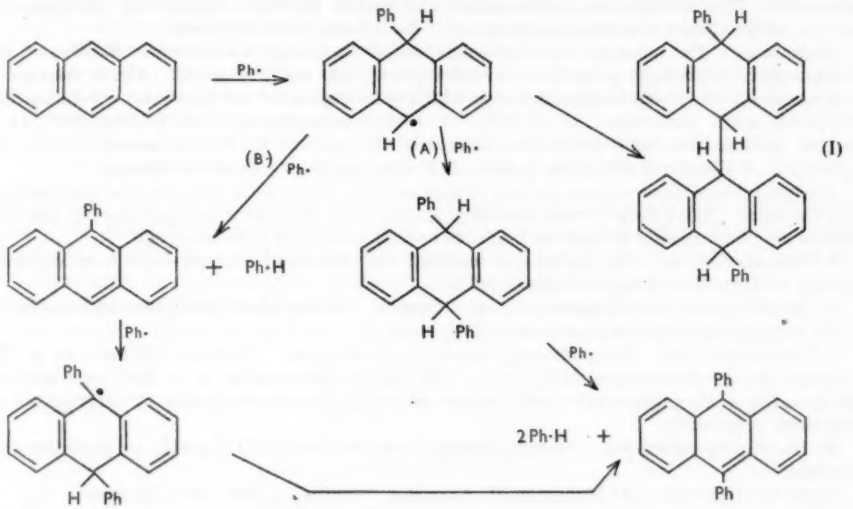
Both 9-methyl- and 9-phenyl-anthracene reacted with phenyl radicals much more readily than did anthracene itself, no starting material being recovered in either case. This accords with the previously reported [14] higher reactivity of *meso*-substituted anthracenes

* We thank Dr. Cadogan for this significant information about his unpublished work.

[8] Waters, *J.*, 1939, 864.
[9] Hanby and Waters, *J.*, 1946, 1029.
[10] Beckwith and Waters, *J.*, 1956, 1108.
[11] *Idem*, *J.*, 1957, 1001.
[12] Dannley and Zaremsky, *J. Amer. Chem. Soc.*, 1955, **77**, 1588.
[13] Hey, Pengilly, and Williams, *J.*, 1956, 1463.
[14] Farenhorst and Kooyman, *Nature*, 1955, **175**, 598.

towards free radicals. 9 : 10-Dimethylanthracene, however, proved unreactive; this agrees with its low inhibitory power in the radical-catalysed autoxidation of benzaldehyde.[15]

An improved method for the preparation of 9-substituted anthracenes is described.



Experimental

Materials.—Anthracene was purified by two distillations from ethylene glycol, followed by recrystallisation from toluene; it had m. p. 218°.

9-*Methylanthracene* (cf. ref. 16). A solution of anthrone in hot benzene (80 ml.) was added slowly to a stirred solution of methylmagnesium iodide [from methyl iodide (36·0 g.) and magnesium (6·0 g.) in ether (50 ml.)]. After addition was complete, the solvent was removed through a small fractionating column until the reflux temperature was 79—80°, the solution then refluxed for ½ hr., and an excess of 50% hydrochloric acid added. The organic layer was washed and dried ($CaCl_2$), the solvent was removed, and the material, in light petroleum, was filtered through alumina. 9-Methylanthracene gave yellow plates (13·0 g.; 83%), m. p. 79—80°, from methanol.

9-Phenylanthracene was prepared similarly from the Grignard compound from bromobenzene (38·0 g.). The crude product in light petroleum–benzene (1 : 1) was filtered through alumina and crystallised from ethanol–benzene, giving 9-phenylanthracene (17·6 g.; 85%), m. p. 154—155°.

9 : 10-Dimethylanthracene, prepared from 9-methylanthracene by formylation followed by reduction,[17] had m. p. 180—181° after chromatography and crystallisation from ethanol.

" AnalaR " acetone was dried over potassium carbonate, then refluxed over anhydrous copper sulphate, and finally fractionated; it had b. p. 56°. Zinc powder was " AnalaR " material.

9 : 10-Dihydro-9 : 10-diphenylanthracene was prepared by the reduction of 9 : 10-diphenylanthracene with sodium and pentanol,[18] and crystallised from light petroleum–benzene; it had m. p. 227°.

Phenylation.—This was always carried out under the same conditions. A typical experiment was as follows: to a solution of anthracene (2·95 g.; 1/60 mole) in acetone (250 ml.), in a 500-ml. flask fitted with a Hershberg stirrer, nitrogen inlet, and condenser ($CaCl_2$ tube),

[15] Turner and Waters, *J.*, 1956, 879.
[16] Krollpfeiffer and Bronscheid, *Ber.*, 1923, **56**, 1617.
[17] Buu-Hoï and Hoán, *J. Org. Chem.*, 1951, **16**, 874.
[18] Willemart, *Bull. Soc. chim. France*, 1942, **9**, 83.

were added benzenediazonium zincichloride (28·0 g.; 1/15 mole) and a small quantity of chalk (to ensure neutrality). While the suspension was stirred, zinc powder (5 g.) was added in small portions. When the initial reaction had subsided, the mixture was heated until a test with " H " acid showed no unchanged diazonium compound, then filtered hot. The acetone was evaporated from the filtrate and the viscous residue repeatedly extracted with hot petroleum. This solution was concentrated and cooled, material crystallising was removed, and the mother-liquor was chromatographed. The results were as follows:

Anthracene. The solution, on cooling, deposited unchanged anthracene. Elution of the chromatogram with light petroleum yielded diphenyl (20 mg.), m. p. 72°, and a mixture of anthracene and 9 : 10-diphenylanthracene which were separated by fractional crystallisation. The yields were: anthracene, in all 39%; 9 : 10-diphenylanthracene, m. p. 248—250°, 11%. Further elution with light petroleum–benzene (6 : 1) gave 9 : 9′ : 10 : 10′-tetrahydro-10 : 10′-diphenyl-9 : 9′-dianthryl (12%), m. p. 255—258° after crystallisation from ethanol.

With ethyl acetate as solvent instead of acetone, the course of the reaction and the products were the same. With fluoroborate instead of zincichloride, the yields dropped sharply, possibly because zinc fluoroborate formed an insoluble coating round the diazonium salt.

9-*Phenylanthracene.* No unchanged material was obtained; the products were diphenyl (25 mg.) and 9 : 10-diphenylanthracene (40%).

9 : 10-*Dihydro*-9 : 10-*diphenylanthracene.* From 9 : 10-dihydro-9 : 10-diphenylanthracene (1 g.) the starting material was recovered in 72% yield.

9-*Methylanthracene.* No unchanged material was obtained. Diphenyl (25 mg.), m. p. 72°, 9-methyl-10-phenylanthracene (44%), m. p. 113°, and its photo-oxide, m. p. 180°, were isolated. The quantity of the photo-oxide could be reduced to 3% but not eliminated by carrying out all operations in the dark.

9 : 10-*Dimethylanthracene.* Starting material was obtained in 71% yield; no products were obtained.

Reference Materials.—9 : 10-Diphenylanthracene [18] had m. p. 248° (from benzene).

9 : 9′ : 10 : 10′-*Tetrahydro*-10 : 10′-*diphenyl*-9 : 9′-*dianthryl.* This was prepared by reducing 10 : 10′-diphenyl-9 : 9′-dianthryl [19] (0·5 g.) with sodium (0·5 g.) in a boiling mixture of pentanol (5 ml.) and toluene (15 ml.); crystallised from benzene it had m. p. 257—258° (yield 50%) (Found: C, 93·9; H, 6·1. $C_{40}H_{30}$ requires C, 94·1; H, 5·9%).

9-*Methyl*-10-*phenylanthracene.* The method involving the conversion of anthrone into 10-phenylanthrone, followed by methylation and dehydration [20] was inferior to the following: A solution of 9-phenylanthracene (1·1 g.) and *N*-methylformanilide (1·75 g.) in *o*-dichlorobenzene (2·5 ml.) was treated carefully with phosphorus oxychloride (1·75 g.). Hydrogen chloride was evolved; the dark red solution was heated at 95° for 20 min. and then cooled, and aqueous sodium acetate (5 g. in 25 ml.) added. The solvent was removed (steam distillation), and the residue was rubbed with 6N-hydrochloric acid to remove methylaniline. 9-*Formyl*-10-*phenylanthracene* formed yellow cubes (0·90 g., 74%), m. p. 165—166° (from benzene) (Found: C, 88·7; H, 5·0. $C_{21}H_{14}O$ requires C, 88·7; H, 5·0%). Infrared absorption: intense band at 5·99 μ. The formyl compound was reduced by the Huang-Minlon procedure to 9-methyl-10-phenylanthracene, m. p. 113°, in 85% yield.

9-Methyl-10-phenylanthracene photo-oxide was prepared [21] by keeping a solution of the hydrocarbon in carbon disulphide in bright sunlight for 2 hr.; it had m. p. 180°.

1 : 2-*Di*-(10-*phenyl*-9-*anthryl*)*ethane* (*cf. ref.* 22). A mixture of 9-bromomethyl-10-phenylanthracene [20] (0·15 g.) and phenyl-lithium [from bromobenzene (1 ml.) and lithium (0·1 g.) in ether (5 ml.)] was refluxed for 1 hr. Ice and water were added to the cooled solution, the ethereal layer was dried ($CaCl_2$), and the solvent removed. 1 : 2-*Di*-(10-*phenyl*-9-*anthryl*)*ethane* (60% yield) formed yellow needles, m. p. 322—323°, from ethanol–benzene (Found: C, 94·1; H, 5·8. $C_{42}H_{30}$ requires C, 94·4; H, 5·6%).

One of us (R. O. C. N.) thanks the Governing Body of Merton College for a Research Fellowship.

The Dyson Perrins Laboratory, Oxford University. [*Received, July* 16*th*, 1957.]

[18] Barnett and Cook, *J.*, 1923, 2631.
[19] Barnett and Matthews, *Ber.*, 1926, **59**, 1429.
[20] Willemart, *Compt. rend.*, 1936, **203**, 1372.
[21] Hall, Lesslie, and Turner, *J.*, 1950, 711.

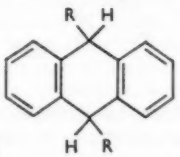
36. *Free-radical Reactions of* 9 : 10-*Diphenylanthracene.*

By A. L. J. Beckwith, R. O. C. Norman, and William A. Waters.

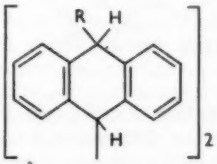
9 : 10-Diphenylanthracene reacts in a terminal ring with both free benzyl and free phenyl radicals to give products which are thought to be 1 : 2-dibenzyl-1 : 2-dihydro- and 1 : 4-dibenzyl-1 : 4-dihydro-9 : 10-diphenylanthracene from the former, and that from the latter has been shown to be 1 : 4 : 9 : 10-tetraphenylanthracene. Methyl and benzyl radicals also add at the *meso*-positions, but the phenyl radical seems to be incapable of doing so, probably for steric reasons.

Analogies to other reactions are discussed, and synthetical work leading to the preparation of 1 : 6-diphenylhexa-2 : 4-diene is described.

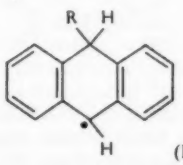
Previously [1,2] it was shown that benzyl radicals add to the *meso*-positions of anthracene to give the adducts (I) and (II) (R = CH_2Ph), hydrogen abstraction from the initial radical adduct (III; R = CH_2Ph) by the benzyl radical not being favoured. Phenyl and methyl radicals, in contrast, give mainly *meso*-substituted products, although the adduct (II; R = Ph or Me) is also formed.[3,4] These radicals are evidently much more effective dehydrogenating agents towards radicals of type (III) than is the benzyl radical.[3]



(I)



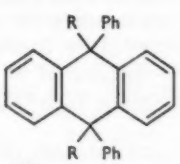
(II)



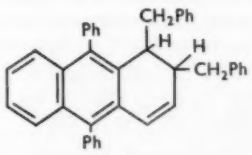
(III)

Acridine also reacts with benzyl radicals in the *meso*-positions to form the dihydro-adduct, but with 9-phenylacridine the attack of the benzyl radical is mainly transferred to the 1-position of a side ring.[5] A similar transfer of reactivity to positions in a side ring has now been established for 9 : 10-diphenylanthracene.

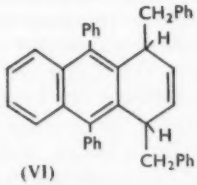
Heating of this hydrocarbon with an excess of *tert.*-butyl peroxide in boiling toluene gives a number of products. That formed in highest yield is 9 : 10-dibenzyl-9 : 10-dihydro-9 : 10-diphenylanthracene (IV; R = CH_2Ph) which, as expected, is not fluorescent and has an ultraviolet spectrum of benzenoid type. Also formed are small amounts of two isomeric hydrocarbons which have ultraviolet spectra of naphthalene type and appear to



(IV)



(V)



(VI)

be 1 : 2-dibenzyl-1 : 2-dihydro-9 : 10-diphenyl (V) and 1 : 4-dibenzyl-1 : 4-dihydro-9 : 10-diphenylanthracene (VI). The former shows spectral resemblances to vinylnaphthalene [6] and even closer similarity with the spectrum of 1 : 2-dihydro-1-hydroxy-2 : 2 : 9 : 10-tetraphenylanthracene,[7] whilst the latter similarly resembles the maleic anhydride adduct of

[1] Norman and Waters, *J.*, 1957, 950.
[2] Beckwith and Waters, *J.*, 1957, 1001.
[3] Norman and Waters, preceding paper.
[4] Beckwith and Waters, *J.*, 1956, 1108.
[5] Waters and Watson, *J.*, 1957, 253.
[6] Laitinen, Miller, and Parks, *J. Amer. Chem. Soc.*, 1947, **69**, 2707.
[7] Étienne and Weill-Raynal, *Bull. Soc. chim. France*, 1953, **20**, 1136.

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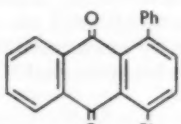
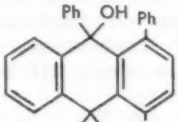
9 : 10-diphenylanthracene, which is known to be a 1 : 4- and not a 9 : 10-adduct.[8] Attempted synthesis of the 1 : 4-dibenzyl adduct by the route effective for 1 : 4 : 9 : 10-tetraphenylanthracene (IX) was unsuccessful. Some new compounds related to 1 : 6-diphenylhexadiene have been synthesised.

Methyl radicals, generated by the decomposition of *tert.*-butyl peroxide in chlorobenzene, give only in poor yield the *meso*-adduct 9 : 10-dihydro-9 : 10-dimethyl-9 : 10-diphenylanthracene (IV; R = Me) together with products derived from attack on the solvent.[9]

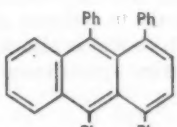
Phenyl radicals, made by the action of zinc powder in acetone on benzenediazonium zincichloride, $(PhN_2)_2ZnCl_4$, do not add to the *meso*-positions of 9 : 10-diphenylanthracene but give a 3% yield of 1 : 4 : 9 : 10-tetraphenylanthracene (IX), identified by the following synthesis. 1 : 4-Diphenylbutadiene was condensed with 1 : 4-naphthaquinone to give the quinone (VII) which was converted into the diphenyl-diol (VIII) with phenylmagnesium bromide and thence into 1 : 4 : 9 : 10-tetraphenylanthracene.[10]



(VII)



(VIII)



(IX)

The proof of this reactivity in the side ring of 9 : 10-diphenylanthracene towards phenyl radicals lends strong support for the formulations, as side-ring adducts, of the two naphthalenic products (V) and (VI) of the reaction between 9 : 10-diphenylanthracene and benzyl radicals. It may be noted that phenyl-radical attack involves hydrogen removal from the initial radical adduct to re-form a stable, aromatic product in which the substituent phenyl groups are conjugated with the rest of the molecule.

Two points of theoretical interest are evident. First, the isolation of 9 : 10-dibenzyl-9 : 10-dihydro-9 : 10-diphenylanthracene and the corresponding dimethyl compound shows that phenyl substituents are not large enough to block the *meso*-carbon atoms from direct attack by both benzyl and methyl radicals. This accords with the observation [11] that 9 : 10-diphenylanthracene is as efficient an inhibiting agent towards the benzoyl peroxide-catalysed autoxidation of benzaldehyde as anthracene itself. Clearly this free-radical attack at the *meso*-positions of 9 : 10-diphenylanthracene must take place at an angle to the plane of the anthracene ring, and would be consistent with benzyl addition to the activated triplet state of the molecule, first postulated by Ingold and Marshall.[12] The failure of the phenyl radical to add to the *meso*-positions of 9 : 10-diphenylanthracene can be attributed to steric effects, for it is impossible to construct a scale model of the corresponding adduct (IV; R = Ph).

Secondly, arylation of the *meso*-positions of anthracene and of acridine must enhance the reactivity towards free radicals of the carbon centres in the side ring, particularly at the *ortho*-carbon atoms. Enhanced side-ring reactivity is exhibited also in the Diels–Alder reactions of these *meso*-arylated compounds [8,13] but from this analogy one need not infer that the Diels–Alder addition proceeds by a homolytic mechanism.

This demonstration of side-ring reactivity in the anthracene series brought about by the blocking of the *meso*-positions is also of interest in connection with the clear evidence of

[8] Cook and Hunter, *J.*, 1953, 4109.
[9] Beckwith and Waters, *J.*, 1957, 1665.
[10] Weizmann, Haskelberg, and Bergmann, *J.*, 1939, 391.
[11] Turner and Waters, *J.*, 1956, 879.
[12] Ingold and Marshall, *J.*, 1926, 3080.
[13] Gillet, *Bull. Soc. chim. France*, 1950, **17**, 1141.

side-ring metabolic attack on anthracene and related carcinogenic hydrocarbons,[14,15] and further investigation is intended.

Experimental

9 : 10-*Diphenylanthracene.*—Anthraquinone (25 g.) was gradually added to a stirred solution of phenyl-lithium [from bromobenzene (52 g.) and lithium (4·5 g.) in ether (20 ml.)] and after 30 minutes' refluxing the mixture was decomposed with aqueous ammonium chloride.[16] The precipitated 9 : 10-dihydroxy-9 : 10-diphenyl-dihydroanthracenes (m. p. *ca.* 180°; 80%) were dried and dissolved in acetic acid (200 ml.), and the solution cautiously treated with phenylhydrazine (20 g.) and refluxed for 30 min. On cooling 9 : 10-diphenylanthracene (m. p. 248° from benzene) was deposited.

Reaction with Methyl Radicals.—9 : 10-Diphenylanthracene (8·7 g.), *tert.*-butyl peroxide (5·5 g.), and chlorobenzene (150 ml.) were refluxed under nitrogen for 50 hr., then concentrated to about 30 ml. and cooled. Impure 9 : 10-diphenylanthracene and a small quantity (0·14 g.) of 9 : 10-dihydro-9 : 10-dimethyl-9 : 10-diphenylanthracene separated. The latter had m. p. 324°, after separation with methanol and crystallisation from much benzene, and was identical with synthetic material (see below). Chromatography of the residue gave more diphenylanthracene (total recovery, 4·3 g.), a little 3 : 3′-dichloro-4 : 4′-dimethyldiphenyl [9] (0·2 g.), and coloured resin containing chlorine.

Reaction with Benzyl Radicals.—9 : 10-Diphenylanthracene (6 g.), *tert.*-butyl peroxide (10 g.), and toluene (150 ml.) were refluxed under nitrogen for 7 days. On cooling, white crystals (0·85 g.) were deposited. These formed minute rhombs, m. p. 312° (from xylene) of 9 : 10-dibenzyl-9 : 10-dihydro-9 : 10-diphenylanthracene, identical with authentic material (see below). The filtrate from separation of this material was evaporated to dryness and extracted with hot methanol (3 × 40 ml.) which removed dibenzyl (5·0 g.). The portion insoluble in cold methanol was dried and then treated with hot light petroleum (100 ml.; b. p. 60—80°). There remained undissolved a mixture of 9 : 10-dibenzyl-9 : 10-dihydro-9 : 10-diphenylanthracene (0·3 g.) and 9 : 10-diphenylanthracene (1·8 g.). Chromatography of the petroleum solution through activated alumina gave successively dibenzyl (0·7 g.), 9 : 10-diphenylanthracene (0·22 g.), crystals (m. p. 176°, from methyl acetate) probably of 1 : 2-dibenzyl-1 : 2-dihydro-9 : 10-diphenylanthracene (0·28 g.) (see below), and needles (m. p. 228°, from methyl acetate) probably of 1 : 4-*dibenzyl*-1 : 4-*dihydro*-9 : 10-*diphenylanthracene* (0·23 g.) (Found: C, 93·6; H, 6·3. $C_{40}H_{32}$ requires C, 93·7; H, 6·3%). The ultraviolet spectrum [max. at 2360 (ε 65,800) and 2950 Å (ε 9500)] of the last compound was similar to that reported for 1 : 4-dihydro-9 : 10-diphenyl-1 : 4-*endo*-αβ-succinic anhydride.[8] On attempted dehydrogenation with sulphur at 240° extensive decomposition occurred.

Reaction with Sodium and Benzyl Chloride.—9 : 10-Diphenylanthracene (4·7 g.), sodium (4 g.), and broken glass (10 g.) were shaken in ether (60 ml.) under nitrogen for 3 days. The dark blue solution was then filtered (glass wool) under nitrogen, and the filtrate was treated dropwise with freshly distilled benzyl chloride until the solution became yellow. Excess of dilute acid was added cautiously. Treatment of the solid product with benzene gave a residue (0·23 g.) of 9 : 10-dibenzyl-9 : 10-dihydro-9 : 10-diphenylanthracene, m. p. and mixed m. p. 312°, and 9 : 10-diphenylanthracene (2·1 g.). Chromatography of the more soluble remainder gave dibenzyl (0·9 g.), more 9 : 10-diphenylanthracene, and an amorphous product (0·6 g.) which slowly crystallised from ether–methanol. Further crystallisation from methyl acetate gave rods, m. p. 178°, probably of 1 : 2-*dibenzyl*-1 : 2-*dihydro*-9 : 10-*diphenylanthracene* (Found: C, 93·5; H, 6·4. $C_{40}H_{32}$ requires C, 93·7; H, 6·3%); light absorption in chloroform, maxima at 2570 (ε 41,200), 2640 (ε 38,700), 2770 (ε 31,000), 2930 (ε 13,600), 3030 (ε 16,750), and 3130 Å (ε 14,850). This absorption is similar to that of vinylnaphthalene [6] and almost identical with that of 1 : 2-dihydro-1-hydroxy-2 : 2 : 9 : 10-tetraphenylanthracene.[7] Finally, 1 : 4-dibenzyl-1 : 4-dihydro-9 : 10-diphenylanthracene (0·07 g.), m. p. 228°, was obtained. The preceding 1 : 2-dihydro-compound was not affected by sulphur at 240° for 2 hr. Treatment with chloranil in boiling xylene gave a 30% yield of an *isomer*, m. p. 164° (Found: C, 93·9; H, 6·3. $C_{40}H_{32}$

[14] Boyland and Levi, *Biochem. J.*, 1935, **29**, 2679.
[15] Berenblum, Crowfoot, Holiday, and Schoental, *Cancer Res.*, 1943, **3**, 151.
[16] Cf. Willemart, *Bull. Soc. chim. France*, 1942, **9**, 83.

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requires C, 93·7; H, 6·3%). This had a different infrared spectrum from the compound of m. p. 178°, and its ultraviolet spectrum in chloroform had maxima at 2570 (ε 46,500), 2640 (ε 45,500), 2760 (ε 37,700), 2900 (ε 19,600), 3020 (ε 21,100), and 3130 Å (ε 17,050).

Reaction with Phenyl Radicals (*cf. ref.* 3).—Benzenediazonium zincichloride (28 g.; 4 mol.) was suspended in dry acetone (200 ml.) in which was dissolved 9 : 10-diphenylanthracene (5·5 g.; 1 mol.). A small quantity of chalk was added, and a stream of dry nitrogen was passed over the system. Zinc powder ("AnalaR") (5 g.) was added in small portions. After the initial reaction was over, the mixture was refluxed for 1 hr. and filtered. The solvent was evaporated and the resulting material was extracted in hot light petroleum. This solution was concentrated to 500 ml. and chromatographed. Elution with light petroleum gave diphenyl (25 mg.) and then 9 : 10-diphenylanthracene (4·41 g.; 80% recovery). Elution with light petroleum–benzene gave 1 : 4 : 9 : 10-tetraphenylanthracene (0·24 g.; 3%), m. p. and mixed m. p. 203—204°, identical with an authentic specimen synthesised as described below.

Preparations of Reference Compounds.—9 : 10-*Dibenzyl*-9 : 10-*dihydro*-9 : 10-*diphenylanthracene.* 9 : 10-Dihydro-9 : 10-dihydroxy-9 : 10-diphenylanthracene (see p. 173) (4 g.) in hot dry chloroform (30 ml.) was treated with gaseous hydrogen chloride; acetic acid (60 ml.) then precipitated 9 : 10-dichloro-9 : 10-dihydro-9 : 10-diphenylanthracene, m. p. 186° (4·8 g.). A mixture of this compound (2·2 g.) in hot benzene and the Grignard reagent from benzyl chloride (10 g.) and magnesium (2 g.) in ether (50 ml.) was refluxed for 4 hr. After decomposition with hydrochloric acid the organic solution was evaporated to dryness and the residue extracted with hot benzene. There remained 9 : 10-*dibenzyl*-9 : 10-*dihydro*-9 : 10-*diphenylanthracene* (40 mg.), rhombs (from toluene), m. p. 312° (Found: C, 93·6; H, 6·4. $C_{40}H_{32}$ requires C, 93·7; H, 6·3%); absorption maximum (in alcohol) at 2650 Å (ε 4450). The remaining benzene solution yielded 9 : 10-diphenylanthracene (0·7 g.) and dibenzyl (1·1 g.).

9 : 10-*Dihydro*-9 : 10-*dimethyl*-9 : 10-*diphenylanthracene.* This was prepared similarly from the above dichloro-compound and methylmagnesium iodide, and formed minute rhombs, m. p. 324° (from benzene) (Found: C, 93·5; H, 6·7. $C_{28}H_{24}$ requires C, 93·3; H, 6·7%); absorption maxima (in chloroform) at 2590 (ε 1450), 2650 (ε 1730), and 2730 Å (ε 1350).

Attempted preparation of 1 : 4-*dibenzyl*-1 : 4-*dihydro*-9 : 10-*diphenylanthracene.* The route envisaged was condensation of 1 : 4-naphthaquinone with 1 : 6-diphenylhexa-2 : 4-diene, but the isomers of the latter which we prepared did not condense with the quinone. The product, m. p. 79°, from reduction of 1 : 6-diphenylhexa-1 : 3 : 5-triene, m. p. 205°,[17] was obtained in very small yield. An isomer was prepared by reduction of 1 : 6-diphenylhex-3-yne-2 : 5-diol as follows: purified acetylene was passed into a solution of the Grignard reagent, from ethyl bromide (30 g.) and magnesium (6·6 g.), in tetrahydrofuran (150 ml.) until the mixture became too viscous to be stirred. Phenylacetaldehyde (25 g.) in tetrahydrofuran (50 ml.) was then added dropwise and the whole was refluxed for 1 hr. and then decomposed with aqueous ammonium chloride. The product, after chromatography, gave a mixture of stereoisomeric 1 : 6-diphenylhex-3-yne-2 : 5-diols (19 g.), m. p. 90°, which were separated by fractional crystallisation from ether–light petroleum (b. p. 40—60°). The less soluble (? meso-)1 : 6-*diphenylhex*-3-*yne*-2 : 5-*diol* had m. p. 105—106° and absorption maxima (in ethanol) at 2130 (ε 11,300), 2480 (ε 221), 2530 (ε 303), 2580 (ε 339), 2640 (ε 303), and 2680 Å (ε 224) (Found: C, 81·3; H, 7·1. $C_{18}H_{18}O_2$ requires C, 81·2; H, 6·8%). The other (? racemic) *isomer* formed needles, m. p. 102—103°, absorption maxima at 2130 (ε 11,500), 2480 (ε 201), 2550 (ε 294), 2580 (ε 374), 2640 (ε 206), and 2680 Å (ε 206), and had a different infrared spectrum (Found: C, 81·0; H, 7·0%). Reduction of the mixture (3 g.) of diols described above with lithium aluminium hydride (1·8 g.) in ether (80 ml.) gave a mixture of 1 : 6-*diphenylhex*-3-*ene*-2 : 5-*diols* (1·9 g.) which was also separated by fractional crystallisation from ether–light petroleum. One (? *meso-trans*) formed plates, m. p. 103—104° (Found: C, 80·5; H, 7·7. $C_{18}H_{20}O_2$ requires C, 80·6; H, 7·5%); absorption maxima (in ethanol) at 2130 (ε 13,100), 2480 (ε 263), 2530 (ε 359), 2590 (ε 434), 2640 (ε 332), and 2680 Å (ε 286); the other (? racemic-*trans*) had m. p. 98—100° (Found: C, 80·7; H, 7·65%) and absorption maxima at 2140 (ε 11,400), 2480 (ε 238), 2530 (ε 355), 2590 (ε 428), 2640 (ε 346), and 2680 Å (ε 292). Dehydration of this mixture with 5% sulphuric acid in acetic acid gave authentic 1 : 6-diphenylhexa-1 : 3 : 5-triene.

Reduction of the mixed acetylene diols (5 g.) in diethylaniline (140 ml.) under nitrogen with lithium aluminium hydride (2 g.) in ether (40 ml.) at 60—70° [18] gave a crystalline mixture

[17] Kuhn and Winterstein, *Helv. Chim. Acta*, 1928, **11**, 123.
[18] Isler, Montavon, Ruegg, and Zeller, *ibid.*, 1956, **39**, 454.

(1·8 g.) of isomeric ethylenic diols and a solution which, after chromatography, gave a (? trans-trans)-1 : 6-*diphenylhexa*-2 : 4-*diene*, needles (from methanol), m. p. 75° (Found: C, 92·0; H 7·7. $C_{18}H_{18}$ requires C, 92·3; H, 7·7%) and, in ethanol, had absorption maxima at 2110 (ε 19,000), 2420 (ε 31,300) and 2690 Å (ε 1950). It was not identical with the reduction product of 1 : 6-diphenylhexa-1 : 3 : 5-triene. (The tentative geometric structures for these compounds are based on examination of infrared spectra but are uncertain because their absorptions overlap those of the phenyl groups.)

1 : 4 : 9 : 10-*Tetraphenylanthracene*. The Diels–Alder reaction between 1 : 4-diphenylbutadiene [19] and 1 : 4-naphthaquinone in nitrobenzene gave 1 : 4-diphenylanthraquinone.[20] The quinone was converted into 9 : 10-dihydro-9 : 10-dihydroxy-1 : 4 : 9 : 10-tetraphenylanthracene with phenylmagnesium bromide, and this was reduced with potassium iodide and sodium hypophosphite in glacial acetic acid to 1 : 4 : 9 : 10-tetraphenylanthracene,[10] m. p. 204—205°.

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THE DYSON PERRINS LABORATORY, OXFORD UNIVERSITY. [*Received, July 16th*, 1957.]

[19] " Organic Syntheses," Collective Volume II, p. 229.
[20] Bergmann, Haskelberg, and Bergmann, *J. Org. Chem.*, 1942, **7**, 303.

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37. *The Reactions of Pyrene with Free Radicals and with Sodium.*

By R. O. C. NORMAN, G. A. THOMPSON, and WILLIAM A. WATERS.

Pyrene reacts with free benzyl and phenyl radicals at the 1-position, *i.e.* that of its highest free-valence number, displaying a reactivity much lower than that of anthracene. Its sodium adduct, however, which has been previously shown to react with carbon dioxide principally at the 4-position, also reacts with benzyl chloride at the 4-position. The difference between the radical reaction and that of the sodium adduct is discussed. The syntheses of several substituted pyrenes are described.

WE have now extended a study of the actions of benzyl [1,2] and phenyl [3] radicals on polycyclic aromatic compounds to pyrene. This hydrocarbon was of interest since its marked inhibiting effect on the autoxidation of benzaldehyde [4] catalysed by benzoyl peroxide is at variance with its low maximum free-valency number F_{max} in the four equivalent positions 1, 3, 6, and 8,[5] and with its moderate methyl radical affinity,[6] though not so greatly at variance with the polarographic half-wave potential [7] or with the electron localisation energy at the 1-position as computed by Dewar.[8]

Theoretical calculations for pyrene are less certain than those for anthracene and phenanthrene derivatives on account of assumptions concerning the electron localisation at the two inner carbon atoms that carry no hydrogen atom. For instance, the uncoupled structure (I) in which the periphery of the molecule retains its complete conjugation may be significant in the reaction between sodium and pyrene.[9] *X*-Ray measurements [10]

[1] Beckwith and Waters, *J.*, 1957, 1001.
[2] Waters and Watson, *J.*, 1957, 253.
[3] Norman and Waters, *J.*, 1958, 167.
[4] Dunn, Waters, and Roitt, *J.*, 1954, 580.
[5] Berthier, Coulson, Greenwood, and Pullman, *Compt. rend.*, 1948, **226**, 1906.
[6] Levy and Szwarc, *J. Amer. Chem. Soc.*, 1955, **77**, 1949.
[7] Bergman, *Trans. Faraday Soc.*, 1954, **50**, 829.
[8] Dewar, *J. Amer. Chem. Soc.*, 1952, **74**, 3357.
[9] Neunhoefer and Woggon, *Annalen*, 1956, **600**, 34.
[10] J. M. Robertson, " Organic Crystals and Molecules," Cornell University Press, 1953, p. 200.

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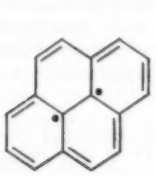
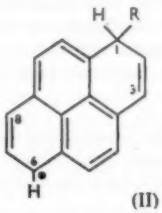
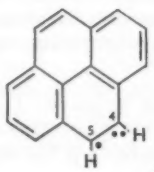
indicate that this inner carbon–carbon bond has a much lower bond order than the average for the other bonds in the molecule. Furthermore, measurements of the free-radical, or electron reactivity of pyrene have not hitherto been supported by isolation and identification of products. The object of this work was to determine the points of free-radical, and of electron, attack on pyrene; it has shown that correlations between measurements of chemical reactivity and theoretical calculations concerning the structure of pyrene cannot be uniformly related because different reaction mechanisms can be involved.



(I)



(II)



(III)

From our work only a comparative estimate of the reactivity of pyrene towards free radicals can be obtained. Whereas reaction of anthracene with benzyl radicals is complete, pyrene is attacked only slightly, and this difference accords well with its lower methyl-radical affinity. The much more reactive phenyl radical gives higher yields of substituted product, as would be expected.

By allowing pyrene to react for two weeks with benzyl radicals in large excess,[1] from decomposing *tert.*-butyl peroxide in boiling toluene, a 3·4% yield of 1-benzylpyrene was obtained and 75% of pyrene recovered. This indicates that benzyl radicals attack, as in structure (II) (the odd electron being distributed between position 6 and others in the molecule), at the carbon atom having the highest F_{max} and the lowest electron localisation energy. Similarly, from the reaction of pyrene with phenyl radicals, produced by the action of zinc powder on a suspension of benzenediazonium zincichloride $(PhN_2)_2ZnCl_4$, in dry acetone,[3] 1-phenylpyrene was obtained together with traces of diphenylpyrenes, probably the 1 : 6- and the 1 : 8-compound. The structures of these 1-substituted pyrenes have been established by relation to the work of Vollmann, Becker, Corell, and Streeck [11] who prepared 1-benzoylpyrene and converted it *via* 1 : 6-dibenzoylpyrene into pyranthrone and by the direct conversion of 1-aminopyrene into 1-phenylpyrene. We have reduced 1-benzoylpyrene directly to the 1-benzylpyrene obtained by the action of benzyl radicals on pyrene, and converted 1-nitropyrene into 1-aminopyrene and thence into pyrene-1-diazonium fluoroborate which when decomposed in benzene in the presence of sodium acetate yielded 1-phenylpyrene, identical with the product of direct phenylation.

Neunhoefer and Woggon [9] obtained 4 : 5-dihydropyrene from the sodium adduct of pyrene and ammonium bromide in liquid ammonia, and by treating the adduct, prepared in an ethereal solution of ammonia, with carbon dioxide they obtained pyrene-4-carboxylic acid as expected if the adduct had the electron-localised structure (III).[9] From the adduct and benzyl chloride, in ether, we obtained 4-benzylpyrene, and have confirmed this structure by making the same compound from pyrene-4-carboxylic acid. A trace of a dibenzylpyrene was also obtained. This, from spectral evidence, appears to be 4 : 9-dibenzylpyrene; it is not 4 : 5-dibenzylpyrene, which we have synthesised unambiguously from pyrene-4 : 5-quinone. The proof of the structure of pyrene-4-carboxylic acid also depends on a sequence relating it to pyrene-4 : 5-quinone.[9] The infrared spectra of these pyrene derivatives, listed below, give further support to these orientations. The ultra-violet spectra are all characteristically of pyrene type.

Establishment of the these structures shows clearly that whilst the electrically neutral free radicals, benzyl and phenyl, attack pyrene at the point of maximum free valence, sodium gives up an electron to pyrene to form a radical-anion which, on the approach of a cationoid

reagent such as carbon dioxide or benzyl chloride, reacts as if the added electron were localised mainly at the carbon–carbon bond of highest bond order, as in structure (III).

It seems therefore that single-electron and neutral free-radical addition to aromatic systems are dissimilar processes and consequently that polarographic redox potentials of aromatic compounds need not be consistent with radical affinities. As yet, however, experimental disagreements with wide theoretical approximations of this type are so few that examples such as the reactivity of pyrene described above, deserve note.

Experimental

Attack of Benzyl Radicals on Pyrene.—Pyrene (6 g.), *tert.*-butyl peroxide (7 g.), and toluene (250 ml.) were refluxed under nitrogen for 2 weeks, more peroxide being added after the first week. After removal of steam-volatile products the residue was chromatographed (Al_2O_3, type H), giving pyrene (4·5 g.) and a yellow gum that darkened in sunlight. Sublimation at 170°/0·02 mm. and crystallisation from methanol gave crystals (0·3 g.), m. p. 89°, identical (mixed m. p., replicate ultraviolet and infrared spectra) with authentic 1-benzylpyrene (see below).

Attack of Sodium and then Benzyl Chloride on Pyrene.—Pyrene (5 g.) in ether (150 ml.) was added to sodium in liquid ammonia (100 ml.), and the ammonia allowed to evaporate slowly in nitrogen. Dry benzyl chloride was then added cautiously until the solution was decolorised. After addition of alcohol, solvents were evaporated, volatile material was removed by steam distillation, and the residue was chromatographed on alumina. It yielded pyrene (2·9 g.), *4-benzylpyrene*, m. p. 170° (0·12 g.) (Found: C, 94·1; H, 5·7. $C_{23}H_{16}$ requires C, 94·5; H, 5·5%), and a much smaller amount of a white solid, m. p. 222—224°, probably impure 4 : 9-dibenzylpyrene (Found: C, 93·2; H, 5·1. $C_{30}H_{22}$ requires C, 94·2; H, 5·8%).

Attack of Phenyl Radicals on Pyrene.—Benzenediazonium zincichloride (28·0 g., 4 mol.) was suspended in dry acetone (200 ml.) in which was dissolved pyrene (3·37 g., 1 mol.); a little chalk was added to ensure neutrality. The mixture, kept in purified dry nitrogen, was stirred vigorously and zinc powder (" AnalaR "; 5 g.) was added in small portions. When the initial reaction had subsided, the mixture was refluxed for 1 hr.; a test with " H " acid was then negative. The solution was filtered, the solvent removed by evaporation, and the residue extracted with light petroleum (b. p. 60—80°). Chromatography of this solution (Al_2O_3, type H) yielded, in order: diphenyl (30 mg.), m. p. 72°, pyrene (1·38 g.; 41%), *1-phenylpyrene* (1·0 g., 21%), m. p. 84° (from methanol) (Found: C, 94·4; H, 5·1. $C_{22}H_{14}$ requires C, 94·9; H, 5·1%), and a mixture of two compounds, separated by fractional crystallisation from ethanol [Found, in compound (*a*), m. p. 209° (0·03 g.): C, 94·8; H, 5·1. In compound (*b*), m. p. 215° (0·04 g.): C, 94·3; H, 5·1. $C_{28}H_{18}$ requires C, 94·9; H, 5·1%].

Syntheses of Reference Compounds.—*1-Benzylpyrene.* Aluminium chloride (2·5 g.) was added gradually to a stirred solution of pyrene (2·5 g.) and benzoyl chloride (1·9 g.) in benzene (25 ml.). After an hour water was added and the mixture distilled in steam. Material extracted from the residue by benzene gave 1-benzoylpyrene (2·4 g.), m. p. 126° (from ethanol); Vollmann *et al.*[11] give 127°. This ketone (2·4 g.) was reduced during 5 hr. by hydrazine hydrate (78% w/w; 1 ml.) and potassium hydroxide (1 g.) in refluxing diethylene glycol (20 ml.), the temperature being kept at 220—240° for the last 3 hr. The mixture was poured into water and extracted with ether, giving 1-benzylpyrene (1·8 g.), m. p. 89° (from methanol) (Found: C, 94·5; H, 5·3. Calc. for $C_{23}H_{16}$: C, 94·5; H, 5·5%): Buu-Hoï, Eckert, and Demerseman [12] give m. p. 91°.

1 : 6- and 1 : 8-Dibenzylpyrene. Pyrene (5 g.) was condensed with an excess of benzoyl chloride, as described by Vollmann *et al.*,[11] and the resulting mixture of 1 : 6-dibenzoylpyrene (1·2 g.), m. p. 237° (lit. 239°), and 1 : 8-dibenzoylpyrene (2·4 g.), m. p. 159—163° (lit. 165°), was separated by crystallisation from acetic acid. Each of these compounds was reduced as described above, and purified chromatographically. *1 : 6-Dibenzylpyrene* had m. p. 194° (Found: C, 93·8; H, 6·0. $C_{30}H_{22}$ requires C, 94·2; H, 5·8%); 1 : 8-dibenzylpyrene which was not rigorously purified had m. p. 184—188°.

[11] Vollmann, Becker, Corell, and Streeck, *Annalen*, 1937, **531**, 1.
[12] Buu-Hoï, Eckert, and Demerseman, *J. Org. Chem.*, 1954, **19**, 726.

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4 : 5-*Dibenzylpyrene*. Pyrene was oxidised with ozone and the resulting 4-formylphenanthrene-5-carboxylic acid was converted into pyrene-4 : 5-quinone (yellow needles; m. p. 307°; lit. 310°) as described by Vollmann *et al.*[11] The quinone (2 g.) in hot dry benzene (500 ml.) was added to the Grignard reagent from benzyl chloride (7 g.) in ether (200 ml.), and the mixture was boiled for 3 hr. The organic product after chromatography gave a mixture (1·2 g.) of the stereoisomers of 4 : 5-dibenzyl-4 : 5-dihydro-4 : 5-dihydroxypyrene, m. p. 105—115°, which was isomerised during 3 hr. by refluxing thionyl chloride, giving 5 : 5-*dibenzyl*-4 : 5-*dihydro*-4-*oxopyrene* (1 g.), m. p. 164° (from light petroleum) (Found: C, 90·6; H, 5·8. $C_{30}H_{22}O$ requires C, 90·5; H, 5·6%). Its spectrum showed ketonic absorption at 5·98 μ. The ketone (150 mg.) was reduced with a large excess of lithium aluminium hydride in ether to the corresponding secondary alcohol which, without purification, was treated with sulphuric acid (0·5 ml.) in acetic acid (10 ml.) to effect the retropinacol shift to 4 : 5-*dibenzylpyrene* (95 mg.), m. p. 158° (from methanol) (Found: C, 94·1; H, 5·9. $C_{30}H_{22}$ requires C, 94·2; H, 5·8%).

4-*Benzylpyrene*. Pyrene (5 g.) in ether (100 ml.) was added to sodium (1·2 g.) in liquid ammonia (100 ml.) under nitrogen, and the ammonia was allowed to evaporate slowly. Carbon dioxide was passed into the red mixture until the deep colour had disappeared. Pyrene-4-carboxylic acid was extracted from the product with aqueous potassium carbonate, precipitated with hydrochloric acid and purified by sublimation at 200°/0·02 mm.; the yield was 1·5 g. (m. p. 256—257°; Neunhoefer and Woggon [9] give 258°). A suspension of the acid (1 g.) in benzene (30 ml.) was refluxed for 30 min. with phosphorus pentachloride (1 equiv.), then aluminium chloride (1·2 g.) was added and the mixture was refluxed for a further 30 min. The resulting benzene solution was washed with water and alkali, then passed through alumina, giving a yellow ketonic (infrared spectrum) gum (0·8 g.) which was reduced with hydrazine and alkali as described for the isomer (above). The resulting 4-*benzylpyrene* (0·4 g.), m. p. 170°, was purified chromatographically; it was identical with the substance obtained by the action of benzyl chloride on the sodium adduct of pyrene.

4-*Benzyl*-sym-*hexahydropyrene and* 4 : 9-*dibenzyl*-sym-*hexahydropyrene*. Pyrene was reduced to *sym*-hexahydropyrene, m. p. 131—132°, with sodium in boiling pentyl alcohol and this was converted into 4-benzoylhexahydropyrene, m. p. 109° (lit. 109°) by the usual procedure.[11] Reduction with hydrazine and alkali, followed by chromatography and crystallisation from methanol, gave 4-*benzyl*-1 : 2 : 3 : 6 : 7 : 8-*hexahydropyrene*, m. p. 65° (Found: C, 92·4; H, 7·4. $C_{23}H_{22}$ requires C, 92·6; H, 7·4%). Treatment of hexahydropyrene with a larger amount of benzoyl chloride gave the 4 : 9-dibenzoylhexahydropyrene, m. p. 272—273° (lit. 273°),[11] which by similar reduction gave 4 : 9-*dibenzyl*-1 : 2 : 3 : 6 : 7 : 8-*hexahydropyrene*, m. p. 211° (from ethanol) (Found: C, 92·4; H, 7·2. $C_{30}H_{28}$ requires C, 92·7; H, 7·3%). Attempted dehydrogenation of these mono- and di-benzoyl- and -benzyl-hexahydropyrenes was unsuccessful.

1-*Phenylpyrene*. 1-Nitropyrene [13] was reduced with palladium–charcoal and hydrazine hydrate in ethanol to 1-aminopyrene, m. p. 117°.[14] To a solution of the diazotised amine was added an excess of saturated aqueous sodium fluoroborate. The precipitated pyrene-1-diazonium fluoroborate was washed with water, ethanol, and finally benzene. The salt (1 g.) was suspended in dry benzene (10 ml.) and anhydrous sodium acetate (0·3 g.) and acetic anhydride (0·1 g.) were added. After 24 hr. at room temperature, during which there was slow evolution of nitrogen, the mixture was refluxed for 2 hr. Water was added, the organic layer dried ($CaCl_2$), the solvent removed by evaporation, and the residue, in light petroleum (b. p. 60—80°), was passed through alumina. 1-*Phenylpyrene* was obtained as plates, m. p. 84°, in 24% yield (Found: C, 94·6; H, 5·1. $C_{22}H_{14}$ requires C, 94·9; H, 5·1%).

Infrared Spectra.—Diphenylpyrenes. Compound (*a*), m. p. 209°, and compound (*b*), m. p. 215°, both showed strong bands corresponding to a monosubstituted benzene, (*a*) at 13·08 and 14·44 μ, (*b*) at 13·08 and 14·20 μ. Each had an intense band corresponding to two adjacent hydrogen atoms in an aromatic system, (*a*) at 11·94 and (*b*) at 11·88 μ. Neither showed any absorption in the range 12·35—13·45 μ which would indicate three adjacent aromatic hydrogen atoms, whereas the spectrum of pyrene itself has a band of medium strength at 13·40 μ, corresponding to its two pairs of three adjacent hydrogen atoms.

Ultraviolet Spectra.—Details are given in the Table.

[13] Bavin and Dewar, *J.*, 1956, 164.
[14] Dewar and Mole, *J.*, 1956, 2556.

Ultraviolet spectra [wavelength in Å (log $\varepsilon_{max.}$ in parentheses)].

Pyrene	—	2400 (4·9)	2640 (4·3)	2750 (4·7)	3190 (4·5)	3350 (4·7)
1-Benzylpyrene	—	2430 (4·8)	2655 (4·4)	2765 (4·7)	3265 (4·4)	3430 (4·6)
4-Benzylpyrene	—	2440 (4·7)	2670 (4·3)	2780 (4·7)	3280 (4·3)	3450 (4·5)
1 : 6-Dibenzylpyrene	—	2450 (4·1)	2680 (3·7)	2790 (4·0)	3340 (3·8)	3500 (4·0)
?4 : 9-Dibenzylpyrene	—	2450 (4·8)	2670 (4·45)	2780 (4·7)	3240 (4·4)	3400 (4·6)
4 : 5-Dibenzylpyrene	—	2450 (4·8)	2670 (4·5)	2780 (4·8)	3260 (4·4)	3420 (4·6)
1-Phenylpyrene	—	2440 (4·8)	2670 (4·5)	2770 (4·7)	—	3400 (4·5)
Diphenylpyrenes:						
(*a*) m. p. 209°	2020 (4·8)	2400 (4·8)	—	2770 (4·7)	—	3420 (4·6)
(*b*) m. p. 215°	2040 (4·8)	2480 (4·7)	2720 (4·5)	2820 (4·7)	—	3510 (4·6)
1 : 2 : 3 : 6 : 7 : 8-Hexahydropyrene	—	2340 (4·8)	2960 (4·0)	—	—	—
4-Benzylhexahydropyrene	—	2380 (4·9)	2980 (4·0)	—	—	—

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38. *The* Euphorbia *Resins. Part X.* The Structural Difference between Euphol and Tirucallol.*

By F. L. WARREN and K. H. WATLING.

Tirucalla-8 : 24-diene has been oxidised to 7 : 11-dioxotirucall-8-enoic acid and the methyl ester subjected to the Grignard reaction with phenylmagnesium bromide. The resulting tertiary alcohol has been dehydrated and treated with *N*-bromosuccinimide, to give 24 : 24-diphenyltrisnortirucalla-8 : 20(22) : 23-triene-7 : 11-dione (V), identical with the corresponding derivative from eupha-8 : 24-diene. Further, compound (V) has been oxidised and then reduced to hexanortirucallane-7 : 11 : 20-trione (XIV) which is almost certainly identical with hexanoreuphane-7 : 11 : 20-trione of Christen, Jeger, and Ruzicka. Thus euphol is 20-*iso*tirucallol (II).

The Barbier–Wieland degradation of the side-chain of euphol (II) is reported and observations on the re-introduction of the 8 : 9-double bond by *N*-bromosuccinimide and by chromic acid are made.

THE structure of euphol was put forward by Barton, McGhie, Pradhan, and Knight [1] and by Jeger and his co-workers.[2] The molecular formula of tirucallol was advanced by Arigoni, Jeger, and Ruzicka [3] as well as by Barbour, Lourens, and ourselves [4] from different evidence. These two triterpenes differed in configuration at $C_{(20)}$, and the orientation at $C_{(17)}$ remained controversial.

Jeger, Ruzicka, and their co-workers [5] have recently demonstrated the α-configuration of the side-chain of tirucallol (I; R′ = OH) by showing that the orientation at $C_{(17)}$ is opposite to that of lanosterol, the stereochemistry of which was rigidly established by Woodward, Patchett, Barton, Ives, and Kelly.[6] Further, Wolff–Kishner reduction of 3β-acetoxytirucall-8-en-21-one (III; R′ = OAc) which gave tirucallenol [3] has now been shown to give also euphenol,[5] the formation of which is attributed to inversion at $C_{(20)}$ only, so that euphol would be (II; R′ = OH). We have now eliminated the asymmetry at $C_{(20)}$ of corresponding derivatives from both tirucallol (I; R′ = OH) and euphol and

* Part IX, *J.*, 1955, 2194.

[1] Barton, McGhie, Pradhan, and Knight, *Chem. and Ind.*, 1954, 1325; *J.*, 1955, 876.
[2] Arigoni, Viterbo, Dunnenberger, Jeger, and Ruzicka, *Helv. Chim. Acta*, 1954, **37**, 2306.
[3] Arigoni, Jeger, and Ruzicka, *ibid.*, 1955, **38**, 222.
[4] Barbour, Lourens, Warren, and Watling, *Chem. and Ind.*, 1955, **226**; *J.*, 1955, 2194.
[5] Menard, Wyler, Hiestand, Arigoni, Jeger, and Ruzicka, *Helv. Chim. Acta*, 1955, **38**, 1517.
[6] Woodward, Patchett, Barton, Ives, and Kelly, *J. Amer. Chem. Soc.*, 1954, **76**, 2852.

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obtained identical products. Euphol, which was first isolated by Newbold and Spring [7] and has been recently reviewed by Jones and Halsall,[8] is completely defined as 20-*iso*-tirucallol (II; R′ = OH).

Tirucallol (tirucalla-8 : 24-dien-3-ol) was oxidised to tirucalladienone, characterised as its 2 : 4-dinitrophenylhydrazone, and then reduced to tirucalladiene. This diene was oxidised with chromic acid to 7 : 11-dioxotrisnortirucall-8-enoic acid (IV; R′ = H). The methyl ester (IV; R′ = Me) was reduced with zinc dust and acetic acid to methyl dioxotrisnortirucallanoate (VIII) which with phenylmagnesium bromide gave 24-hydroxy-24 : 24-diphenyltrisnortirucallane-7 : 11-dione (IX). This hydroxy-compound was readily dehydrated in boiling benzene containing a little iodine to the 23-ene (X) which with *N*-bromosuccinimide followed by boiling pyridine gave 24 : 24-diphenyltrisnortirucalla-8 : 20(22) : 23-triene-7 : 11-dione (V), m. p. 216—217°, $[\alpha]_D$ +21·6°, $\lambda_{max.}$ 301 mμ (log ε 4·61) [shoulder at λ 275 mμ (log ε 4·52)], with a strong band at 1671 cm.$^{-1}$ characteristic of the 1 : 4-diketo-ene system. Further, compound (V) was readily reduced with zinc dust and acetic acid to 24 : 24-diphenyltrisnortirucalla-20(22) : 23-diene-7 : 11-dione (XI), m. p. 199—200°, $[\alpha]_D$ −137°.

A similar series of reactions on eupha-8 : 24-diene reported by Christen, Jeger, and Ruzicka [9] confirms the physical properties of all the products. The action of *N*-bromosuccinimide on 24 : 24-diphenyltrisnoreuph-23-ene-7 : 11-dione and dehydration of the product gave the yellow compound, m. p. 214—216°, $[\alpha]_D$ +21·6°, which, however, is 24 : 24-diphenyltrisnoreupha-8 : 20(22) : 23-triene-7 : 11-dione (V) and not the diene (XI) as previously reported.[9] By using two equivalents of *N*-bromosuccinimide higher yields were obtained and the difficult separation was avoided. This trisnoreuphatriene (V) showed ultraviolet and infrared absorption characteristic of the diketone structure and its infrared spectrum was identical with that of the trisnortirucallatriene (V) with which it showed no melting-point depression.

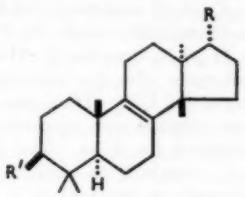
Oxidation of 24 : 24-diphenyltrisnortirucalla-8 : 20(22) : 23-triene-7 : 11-dione (V) with chromic acid gave hexanortirucall-8-ene-7 : 11 : 20-triene (VII) as yellow needles, m. p. 189—190° which was reduced to the corresponding hexanortirucallanetrione (XIV), m. p. 223—225°, $[\alpha]_D$ −244°. This compound (XIV) is almost certainly identical with hexanoreuphanetrione, m. p. 223—225°, $[\alpha]_D$ −232°, of Christen, Jeger, and Ruzicka,[9] and was further characterised as its 2 : 4-dinitrophenylhydrazone. Compound (XIV) could not, however, have been obtained directly from pure 24 : 24-diphenyltrisnoreupha-8 : 20(22) : 23-triene-7 : 11-dione (V), which is now the structure assigned to the starting material; and it is probable that these authors oxidised the mixture of diene and triene or omitted to record the reduction stage.

The action of *N*-bromosuccinimide in re-introducing the 8 : 9-double bond was repeated on 7 : 11-dioxoeuphanyl acetate [10] to give 7 : 11-dioxoeuph-8-enyl acetate.[11]

Before this reaction with *N*-bromosuccinimide was fully appreciated, and in view of the difficulties associated with the isolation of the large quantities of tirucallol necessary for the separation of the butadiene (XII), a study was made of the Barbier–Wieland stepwise degradation of the side-chain of euphol. 24 : 24-Diphenyltrisnoreuph-23-ene-7 : 11-dione (X) was oxidised with chromic acid to 7 : 11-dioxotetranoreuph-8-enoic acid (VI; R′ = H), and the methyl ester (VI; R′ = Me) reduced to methyl 7 : 11-dioxotetranoreuphanoate (XII; R′ = Me). The Grignard reaction with phenylmagnesium bromide on compound (XII; R′ = Me), dehydration of the product, and then oxidation with chromic acid gave a yellow oily acid, which on reduction with zinc dust and acetic acid yielded 7 : 11-dioxopentanoreuphanoic acid (XIII; R′ = H) characterised further

[7] Newbold and Spring, *J.*, 1944, 249.
[8] Jones and Halsall, *Fortschr. Chem. org. Naturstoffe*, 1955, **12**, 101; see also ref. 1.
[9] Christen, Jeger, and Ruzicka, *Helv. Chim. Acta*, 1951, **34**, 1675.
[10] Christen, Dunnenberger, Roth, Heussen, and Jeger, *ibid.*, 1952, **35**, 1771.
[11] Haines and Warren, *J.*, 1950, 1563.

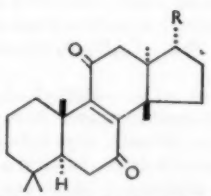
as its methyl ester. Oxidation of 24 : 24-diphenyltrisnortirucall-23-ene-7 : 11-dione (X) also gave only an oily acid; but reduction of the acid resulted in crystalline 7 : 11-dioxotetranortirucallanoic acid (XII; R′ = H), isolated also as its methyl ester.



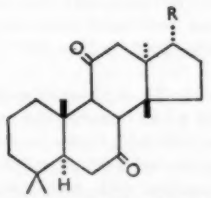
(I) R = Me–C(H)–CH_2·CH_2·CH:CMe_2 (Tirucallol)

(II) R = H–C(Me)–CH_2·CH_2·CH:CMe_2 (Euphol)

(III) R = O:CH–C(H)–$[CH_2]_3$·$CHMe_2$



(IV) R = –CHMe·CH_2·CH_2·CO_2R′
(V) R = –CMe:CH·CH:CPh_2
(VI) R = –CHMe·CH_2·CO_2R′
(VII) R = –COMe



(VIII) R = –CHMe·CH_2·CH_2·CO_2Me
(IX) R = –CHMe·CH_2·CH_2·CPh_2·OH
(X) R = –CHMe·CH_2·CH:CPh_2
(XI) R = –CMe:CH·CH:CPh_2
(XII) R = –CHMe·CH_2·CO_2R′
(XIII) R = –CHMe·CO_2R′
(XIV) R = –COMe

It is to be noted that the chromic acid oxidation of the diphenylethylenes from tirucallol and euphol to corresponding acids is accompanied by partial restoration of the 8 : 9-double bond, and the resulting mixture was difficult to separate. Reduction of the mixture with zinc dust and acetic acid immediately gave crystalline acids. The dehydrogenation of euphane-7 : 11-diones with *N*-bromosuccinimide and with chromic acid parallels the dehydrogenation by selenium dioxide and by aerial oxidation accelerated by alkaline conditions reported by Barton and McGhie and their co-workers.[12,1] These are other examples of the difference between euphane-7 : 11-dione and lanostane-7 : 11-dione series which have rings B/C *cis*- and *trans*-fused respectively.

Experimental

Rotations are for $CHCl_3$ solutions. Ultraviolet data were determined by Marjorie E. von Klemperer, and infrared spectra by Mr. A. J. Rossouw. Microanalyses were by Yvonne Merchant, analytical samples being dried at 100°/0·1 mm. for 6 hr. unless otherwise stated.

Tirucalla-8 : 24-*dien*-3-*one*.—Tirucall-8-en-3-ol (3·2 g.), benzene (200 ml.), chromic acid

[12] Knight and McGhie, *Chem. and Ind.*, 1953, 920; 1954, 24.

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(4 g.), water (40 ml.), and acetic acid (100 ml.) were stirred for 36 hr. at room temperature. The neutral fraction (3·2 g.) in light petroleum was chromatographed over alumina (70 g.; Grade I); the resulting colourless oil, dissolved in hot methanol, deposited an oil on cooling. The mother-liquors gave after 48 hr. *tirucalla*-8 : 24-*dien*-3-*one* as laminæ, m. p. 62°, $[\alpha]_D^{20}$ +13·7° (Found: C, 84·8; H, 11·5. $C_{30}H_{48}O$ requires C, 84·8; H, 11·4%). The 2 : 4-*dinitrophenylhydrazone* crystallised from methanol–chloroform (6 : 1) as orange laminæ, m. p. 175—176° (Found: C, 71·5; H, 8·9. $C_{36}H_{52}O_4N_4$ requires C, 71·5; H, 8·7%).

Tirucalla-8 : 24-*diene*.—Tirucalladienone (2·4 g.), absolute alcohol (100 ml.), and 50% hydrazine hydrate (2 ml.) were refluxed for 1 hr. Diethylene glycol (100 ml.) and potassium hydroxide (2 g.) were added, and the solution was concentrated under reflux until the temperature reached 200° and then refluxed for 4 hr. The product in light petroleum was chromatographed over alumina (50 g.; Grade I) to yield a colourless oil (2 g.). The sample was sublimed to give fine needles of *tirucalla*-8 : 24-*diene*, m. p. 54°, $[\alpha]_D^{24}$ −21° (Found: C, 88·3; H, 12·5. $C_{30}H_{50}$ requires C, 87·7; H, 12·3%).

7 : 11-*Dioxotrisnortirucall*-8-*enoic Acid* (IV).—Tirucalladiene (2 g.), chloroform (3 ml.), acetic acid (100 ml.), chromium trioxide (4 g.), and water (5 ml.) were kept at 50—60° for 4 hr. and set aside at room temperature overnight. The solution was worked up in the usual way. The solid acid fraction (1·8 g.), crystallised three times from methanol, gave 7 : 11-*dioxotrisnortirucall*-8-*enoic acid* as yellow needles, m. p. 268—270°, $[\alpha]_D^{19}$ −16°. A sample was dried at 76° for 6 hr. for analysis (Found: C, 75·9; H, 9·75. $C_{27}H_{40}O_4$ requires C, 75·7; H, 9·4%) Action of diazomethane on the acid and recrystallisation three times from methanol gave the *methyl ester* as yellow needles, m. p. 171—172°, $[\alpha]_D^{19}$ −16·5° (Found: C, 76·0; H, 9·7. $C_{28}H_{42}O_4$ requires C, 76·0; H, 9·6%).

Methyl 7 : 11-*Dioxotrisnortirucallanoate* (VIII).—Methyl dioxotrisnortirucallenoate (2 g.), glacial acetic acid (100 ml.), and zinc dust (3 g.) were refluxed for 1 hr. The solid product was recrystallised from methanol–chloroform (10 : 1), to give *methyl dioxotrisnortirucallanoate* as needles, m. p. 258—260°, $[\alpha]_D^{19}$ −176° (Found: C, 75·3; H, 10·2. $C_{28}H_{44}O_4$ requires C, 75·6; H, 10·0%).

24-*Hydroxy*-24 : 24-*diphenyltrisnortirucallane*-7 : 11-*dione* (IX).—Methyl dioxotrisnortirucallanoate (3·2 g.) in benzene (50 ml.) and the Grignard reagent, prepared from magnesium (3·8 g.), dry ether (100 ml.), bromobenzene (25 g.), and benzene (100 ml.), were refluxed for 4 hr. The complex was treated with 2N-sulphuric acid and extracted with ether, to yield a gum which solidified on lixiviation with methanol which dissolved the diphenyl. Three crystallisations from acetone gave 24-*hydroxy*-24 : 24-*diphenyltrisnortirucallane*-7 : 11-*dione* as needles, m. p. 210—212°, $[\alpha]_D^{20}$ −113° (Found: C, 82·3; H, 9·4. $C_{39}H_{52}O_3$ requires C, 82·35; H, 9·2%).

24 : 24-*Diphenyltrisnortirucall*-23-*ene*-7 : 11-*dione* (X).—The hydroxy-compound, iodine (100 mg.), and benzene (100 ml.) were refluxed for 1 hr. The product, crystallised three times from methanol–chloroform (6 : 1), gave 24 : 24-*diphenyltrisnortirucall*-23-*ene*-7 : 11-*dione* as laminæ, m. p. 196—197°, $[\alpha]_D^{19}$ −163° (Found: C, 85·0; H, 9·5. $C_{39}H_{50}O_3$ requires C, 85·0; H, 9·2%).

24 : 24-*Diphenyltrisnortirucall*-8 : 20(22) : 23-*triene*-7 : 11-*dione* (V).—Diphenyltrisnortirucallenedione (3·0 g.), dry carbon tetrachloride (100 ml.), and 85% *N*-bromosuccinimide (2·5 g.) were refluxed with slow distillation for 20 min. in a quartz flask in bright sunlight. Copious evolution of hydrogen bromide started after 5 min. and ceased after 20 min. The solution, filtered and evaporated under reduced pressure, gave an oil which was heated with pyridine at 100° for 1 hr. The product in ether was washed with acid, the solvent evaporated, and the residue crystallised twice from acetone, to give 24 : 24-*diphenyltrisnortirucalla*-8 : 20(22) : 23-*triene*-7 : 11-*dione* (1·3 g.) as stout yellow needles, m. p. 216—217°, $[\alpha]_D^{20}$ +21·6°, $\lambda_{max.}$ 301 mμ (log ε 4·61) with a shoulder at 275 mμ (log ε 4·52), showing absorption at 1671 cm.$^{-1}$ (Found: C, 86·0; H, 8·45. $C_{39}H_{46}O_3$ requires C, 85·7; H, 8·5%).

24 : 24-*Diphenyltrisnortirucalla*-20(22) : 23-*diene*-7 : 11-*dione* (XI).—The above triene (200 mg.), glacial acetic acid (40 ml.), and zinc dust (0·4 g.) were refluxed for 30 min. The product, crystallised five times from methanol, gave 24 : 24-*diphenyltrisnortirucalla*-20(22) : 23-*diene*-7 : 11-*dione* as silky needles, m. p. 199—200°, $[\alpha]_D^{20}$ −137°, $\lambda_{max.}$ 305 mμ (log ε 4·36), $\nu_{max.}$ 1700 cm.$^{-1}$ (Found: C, 85·4; H, 9·1. $C_{39}H_{48}O_3$ requires C, 85·35; H, 8·8%).

7 : 11-*Dioxotetranortirucallanoic Acid* (XII; R′ = H).—Diphenyltrisnortirucallenedione (2 g.) in carbon tetrachloride (20 ml.) was added to chromium trioxide (3 g.), water (3 ml.), and acetic acid (190 ml.) at 0°, and the temperature allowed to rise to 40° at which it was maintained

for 4 hr. The oily product was reduced with zinc dust and boiling acetic acid. The solid product, crystallised three times from methanol, gave 7 : 11-*dioxotetranortirucallanoic acid* as fine needles, m. p. 212—214°, $[\alpha]_D^{22}$ −157° (Found: C, 74·5; H, 10·0. $C_{26}H_{40}O_4$ requires C, 75·0; H, 9·7%). Esterification with methanol and dry hydrogen chloride and crystallisation four times from methanol gave the *methyl ester* as fine needles, m. p. 216—217°, $[\alpha]_D^{22}$ −169° (Found: C, 75·5; H, 9·9. $C_{27}H_{42}O_4$ requires C, 75·3; H, 9·8%).

24 : 24-*Diphenyltrisnoreupha*-8 : 20(22) : 23-*triene*-7 : 11-*dione* (V).—This was prepared from 24 : 24-diphenyltrisnoreuph-23-ene-7 : 11-dione [9] (3 g.) and 90% *N*-bromosuccinimide (1·2 g.) as described for the tirucallatriene derivative. The oil was chromatographed in light petroleum–benzene (3 : 1) over alumina (60 g.) to give an oil (2 g.) which was rechromatographed. The first 300 ml. eluted a yellow gum (0·7 g.) and the next 500 ml. gave a yellow oil (1·1 g.) which, crystallised three times from methanol, gave 24 : 24-*diphenyltrisnoreupha*-8 : 20(22) : 23-*triene*-7 : 11-*dione* as yellow needles, m. p. 214—216°, $[\alpha]_D^{22}$ +21·6° (Found: C, 85·8; H, 8·8. $C_{39}H_{46}O_2$ requires C, 85·7; H, 8·5%). Christen *et al.*[9] give m. p. 212—213°, $[\alpha]_D$ +20°, for (XI).

7 : 11-*Dioxotetranoreuph*-8-*enoic Acid* (VI).—Diphenyltrisnoreuphenedione (8 g.) in carbon tetrachloride (30 ml.) was treated with chromium trioxide (8 ml.) in acetic acid (270 ml.) and water (3 ml.) at 0° and set aside at 20° overnight. The acid product was an oil (5 g.) which, crystallised three times from methanol, gave 7 : 11-*dioxotetranoreuph*-8-*enoic acid* as yellow needles, m. p. 230—232°, $[\alpha]_D^{20}$ +10° (Found: C, 74·8; H, 9·3. $C_{26}H_{38}O_4$ requires C, 75·3; H, 9·2%). Esterification with methanol and hydrogen chloride and four crystallisations from methanol gave the *methyl ester* as yellow needles, m. p. 140—142°, $[\alpha]_D^{22}$ +9·5° (Found, after drying at 76°/0·1 mm.: C, 75·8; H, 9·6. $C_{27}H_{40}O_4$ requires C, 75·7; H, 9·4%).

Methyl 7 : 11-*Dioxotetranoreuphanoate* (XII; R′ = Me).—The above ester was reduced with zinc dust and acetic acid. The solid product, crystallised three times from methanol, gave *methyl* 7 : 11-*dioxotetranoreuphanoate* as needles, m. p. 217—218°, $[\alpha]_D^{20}$ −164° (Found: C, 75·25; H, 10·0. $C_{27}H_{42}O_4$ requires C, 75·3; H, 9·8%).

7 : 11-*Dioxopentanoreuphanoic Acid* (XIII; R′ = H).—Methyl dioxotetranoreuphanoate (10 g.) was treated with phenylmagnesium bromide as described above and refluxed for 8 hr. The brown oily product was refluxed with glacial acetic acid for 1 hr. and steam-distilled to remove diphenyl. The residual oil in light petroleum–benzene (3 : 1) was chromatographed over alumina (200 g.). The eluant (1·5 l.) gave an oil (6 g.) which failed to crystallise and was oxidised with chromium trioxide as described above. The acid fraction failed to crystallise and was reduced with zinc dust and acetic acid. The solid product in benzene was chromatographed over alumina (30 g.; Grade II) and crystallised three times from methanol, to give 7 : 11-*dioxopentanoreuphanoic acid* as needles, m. p. 234—236°, $[\alpha]_D^{20}$ −144° (Found: C, 74·8; H, 9·7. $C_{25}H_{38}O_4$ requires C, 74·6; H, 9·5%). Esterified with diazomethane, chromatographed in light petroleum over alumina (grade II), and crystallised three times from methanol, this gave the *methyl ester* as needles, m. p. 196—197°, $[\alpha]_D^{20}$ −103° (Found, after drying at 120°/0·1 mm.: C, 75·0; H, 9·8. $C_{26}H_{40}O_4$ requires C, 75·0; H, 9·7%).

Hexanortirucall-8-*ene*-7 : 11 : 20-*trione* (VII).—Diphenyltrisnortirucallatrienedione (1·3 g.) in carbon tetrachloride (20 ml.) was treated at 0° with chromium trioxide (2·5 g.), water (5 ml.), and acetic acid (150 ml.). The solution was set aside at 40° for 4 hr. The neutral oil (1·2 g.) in benzene was steam-distilled. The residual solid, crystallised three times from methanol, gave *hexanortirucall*-8-*ene*-7 : 11 : 20-*trione* as yellow needles, m. p. 189—190°, $[\alpha]_D^{17}$ −34° (Found: C, 78·1; H, 9·6. $C_{24}H_{34}O_3$ requires C, 77·8; H, 9·25%).

Hexanortirucallane-7 : 11 : 20-*trione* (XIV).—Reduction of hexanortirucallenetrione with zinc dust and acetic acid and four crystallisations of the product from methanol and one from acetone gave hexanortirucallane-7 : 11 : 20-trione as needles, m. p. 223—225°, $[\alpha]_D^{23}$ −244° (Found: C, 77·6; H, 10·05. Calc. for $C_{24}H_{36}O_3$: C, 77·4; H, 9·7%). The 2 : 4-*dinitrophenylhydrazone* crystallised from methanol–chloroform in orange needles, m. p. 251—253° (Found: C, 65·2; H, 7·35. $C_{30}H_{40}O_6N_4$ requires C, 65·2; H, 7·3%).

Dioxoeuphanyl Acetate.—Christen *et al.*[10] give m. p. 156—157°, $[\alpha]_D$ −132°. Prepared by the same method the dioxoeuphanyl acetate crystallised from methanol in plates, $[\alpha]_D^{22}$ −127° (*c* 0·7) (Found: C, 77·0; H, 10·4. Calc. for $C_{32}H_{52}O_4$: C, 76·8; H, 10·4%). In a capillary tube these melted on rapid heating at 131—132°, whilst with slow heating there was partial melting at 132° and flowing at 157°. Slow heating on Kofler stage between crossed Nicol prisms showed m. p. 130—132° with immediate solidification to birefringent crystals, m. p. 144—152°.

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N-Bromosuccinimide and 7 : 11-Dioxoeuphanyl Acetate.—Dioxoeuphanyl acetate [10] (3·2 g.), m. p. 131°, was treated with *N*-bromosuccinimide (1·2 g.) and then with pyridine as above. The product was chromatographed over alumina with light petroleum and crystallised from methanol, to give 7 : 11-dioxoeuph-8-enyl acetate, m. p. 112°, undepressed on admixture with an authentic specimen.[11]

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39. *Adsorption by Oxide Gels from Liquid Mixtures containing Nitrogenous Bases.*

By J. J. KIPLING and D. B. PEAKALL.

Adsorption at 20° on alumina and on silica gel from liquid mixtures of pyridine, piperidine, or *n*-butylamine with a hydrocarbon involves two processes. Irreversible adsorption of the base occurs on a fraction of the surface, possibly owing to the formation of weak chemical bonds to the aluminium or silicon atoms, the strength of the bond being related to the basic strength of each adsorbate. Subsequent physical adsorption is competitive between the base and the hydrocarbon. The individual isotherms are obtained on the assumption that physical adsorption is unimolecular.

AT room temperature, slow chemisorption of the lower aliphatic alcohols by alumina, silica gel, and titania gel takes place provided that oxide ions occur at the surface. Measurements on vapour-phase adsorption showed that chemisorption proceeded until all accessible oxide ions had taken up alcohol.[1] Similar chemisorption occurs from liquid mixtures of the alcohol and an indifferent hydrocarbon such as benzene,[2] which may be of significance in chromatography.

As the chromatographic behaviour of nitrogenous bases is also of interest, we examined the adsorption of pyridine, piperidine, and *n*-butylamine severally from mixtures with either benzene or *cyclo*hexane. Each base was strongly adsorbed, so we could not analyse some of the isotherms of concentration change into reasonable individual isotherms by our usual method.[1] We therefore proceeded as for the alcohols to determine whether the bases were chemisorbed.[2] Some experiments were extended to ammonia, just as some of the work on alcohols was extended to water.

Vapour-phase Experiments.—The solids were saturated with the bases, and vapour-phase desorption was then carried out. The results (Table 1) show that significant irreversible adsorption takes place at 20°. In the cases examined the residual adsorption is less at 60° than at 20°. (The rate of desorption falls to zero in each case. The possibility that the low vapour pressure of the adsorbed bases might result in desorption's continuing at a very low rate seems most unlikely as a limit to desorption is also found with ammonia, which has a vapour pressure of some 8½ atm. at 20°.) Chemisorption of the bases is completed more quickly than that of the alcohols; " irreversible adsorption " of the bases reaches a maximum within 24 hours' contact with the solid, whereas up to a week is required for the alcohols.

Isosteric heats of adsorption were also obtained from the 20° and 60° isotherms of adsorption of pyridine and of ammonia on boehmite. These are given in Table 2, where a comparison is made with the corresponding heats of adsorption of benzene and *cyclo*hexane which are undoubtedly held by physical forces only. The values for the bases

[1] Kipling and Peakall, *J.*, 1956, 4828.
[2] *Idem, J.*, 1957, 834, 4054.

are not only higher than those for the hydrocarbons, but also rise rapidly with fall in surface coverage, whereas the latter values rise very little. The contrast between the two pairs of adsorbates is further emphasised by evaluating the " net " heat of adsorption,

TABLE 1. *Vapour-phase desorption of bases.*

Solid	Vapour	Time of contact (days)	Residual amount adsorbed (mmoles/g.)	Solid	Vapour	Time of contact (days)	Residual amount adsorbed (mmoles/g.)
Boehmite	Bu^nNH_2	1	0·52	" Gibbsite "	C_5H_5N	1	0·35
	$C_5H_{11}N$	1	0·65		C_5H_5N	1 *	0·16
	C_5H_5N	1	0·44				
	C_5H_5N	7	0·44	Silica gel-I	NH_3	3	1·54
	C_5H_5N	1 *	0·22		Bu^nNH_2	1	1·12
					$C_5H_{11}N$	1	1·38
γ-Al_2O_3-I	NH_3	3	0·76		C_5H_5N	1	0·96
	Bu^nNH_2	1	0·61		C_5H_5N	1 *	0·34
	$C_5H_{11}N$	1	0·73		C_5H_5N	7	0·95
	C_5H_5N	1	0·42				
	C_5H_5N	1 *	0·16	Silica gel-II	C_5H_5N	1	1·03

Desorption was continued until no further removal of adsorbate could be detected. The temperatures were 20° except for those marked * which were 60°.

TABLE 2. *Isosteric heats of adsorption on boehmite (kcal./mole adsorbed).*

Surface covered (%)	E_x	$E_x - E_L$	Surface covered (%)	E_x	$E_x - E_L$	Surface covered (%)	E_x	$E_x - E_L$	Surface covered (%)	E_x	$E_x - E_L$
Ammonia			Pyridine			Benzene			*cyclo*Hexane		
87	15·4	10·4	76	18·1	9·4	43	10·1	2·2	38	9·7	1·9
94	12·7	7·7	85	16·8	8·1	54	9·8	1·9	55	9·6	1·8
98	11·9	6·9	93	15·2	6·5	75	9·3	1·4	77	9·4	1·6
						97	9·2	1·3	89	9·3	1·5

($E_x - E_L$), *i.e.*, by subtracting from the total heat of adsorption (E_x) the latent heat of condensation of the vapour (E_L). The heats of adsorption of the bases are so high that at least part of the adsorption must be other than physical. In particular, the values of E_x for ammonia are higher than the maximum for physical adsorption given by Trapnell.[3] The values of ($E_x - E_L$) thus obtained are considerably higher than those obtained from the term c of the BET equation. The values for benzene, however, agree well with those obtained calorimetrically by Gregg and Wheatley,[4] and those for the bases are close to Bastick's calorimetric values for adsorption of ammonia on silica gel.[5] It may thus be questioned whether the term c has its usual significance when mixed physical and chemical adsorption takes place.

Dobay, Fu, and Bartell [6] found similar high heats of adsorption for alkylamines on silica gel and concluded that adsorption in these systems could not be entirely physical. The strong adsorption of such bases by oxide gels may well be general, for Brown and Foster have shown that it occurs with ferric oxide gel.[7] They recorded desorption isotherms, but unfortunately not down to zero pressure, though this may indicate the difficulty of desorption compared with normal systems.

Liquid-phase Experiments.—In the liquid-phase experiments, the bases were adsorbed from mixtures with either benzene or *cyclo*hexane. Data are given in Fig. 1 and Tables 3—5 for the isotherms of concentration change. The vapour-phase experiments show

[3] Trapnell, " Chemisorption," Butterworths, London, 1955.
[4] Gregg and Wheatley, " Proc. 2nd International Congress of Surface Chemistry," Butterworths, London 1957.
[5] Bastick, *Compt. rend.*, 1952, **234**, 1279.
[6] Dobay, Fu, and Bartell, *J. Amer. Chem. Soc.*, 1951, **73**, 308, cf. Dobay and Bartell, *ibid.*, 1950, **72**, 4388.
[7] Brown and Foster, *J.*, 1952, 1139.

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what allowance must be made for irreversible adsorption, and the residual change in concentration can then be apportioned to the physical adsorption of the individual components. The resulting individual isotherms are given in Figs. 2 and 3 and Tables 6—8.

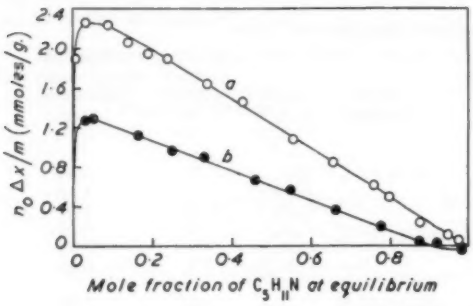

FIG. 1. *Isotherms of concentration change for adsorption at 20° from mixtures of piperidine and* cyclo*hexane on (a) silica gel and (b) boehmite.*

Δx is the decrease in mole fraction of the first-named component due to adsorption when n_0 mmoles of liquid are brought into contact with m g. of solid.

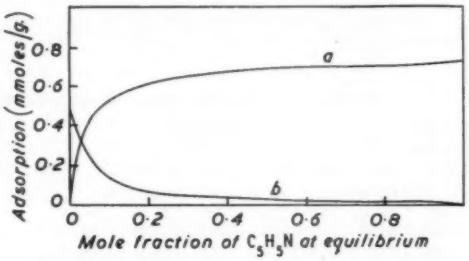

FIG. 2. *Physical adsorption (individual isotherms) by* γ-Al_2O_3 *at 20° from mixtures of (a) pyridine and (b)* cyclo*hexane.*

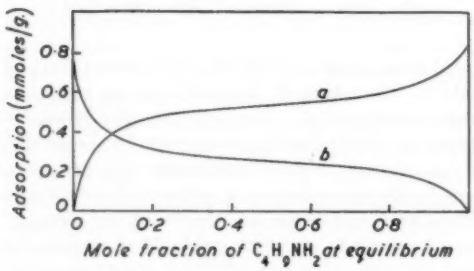

FIG. 3. *Physical adsorption (individual isotherms) by* γ-Al_2O_3 *at 20° from mixtures of (a)* n*-butylamine and (b) benzene.*

TABLE 3. *Adsorption from mixtures of pyridine and* cyclo*hexane; A, mole fraction of pyridine at equilibrium; B,* $n_0\Delta x/m$ *(mmoles/g.).*

A	*B*	*A*	*B*	*A*	*B*	*A*	*B*	*A*	*B*
Boehmite, 20°		Silica gel, 20°		Boehmite, 60°		Silica gel, 60°		γ-Alumina, 20°	
0·03	1·41	0·02	2·64	0·07	1·20	0·01	1·83	0·04	0·80
0·07	1·44	0·06	3·07	0·17	1·19	0·05	2·70	0·10	0·84
0·14	1·38	0·11	3·19	0·26	1·06	0·09	2·90	0·18	0·83
0·29	1·16	0·15	3·14	0·32	0·94	0·14	2·76	0·29	0·74
0·37	1·02	0·24	2·95	0·40	0·84	0·19	2·78	0·38	0·63
0·48	0·82	0·33	2·65	0·48	0·71	0·30	2·51	0·50	0·56
0·59	0·66	0·45	2·22	0·60	0·53	0·37	2·24	0·59	0·46
0·69	0·46	0·55	1·84	0·65	0·49	0·40	2·06	0·68	0·36
0·77	0·35	0·66	1·40	0·71	0·34	0·45	2·00	0·76	0·24
0·83	0·21	0·72	1·05	0·80	0·20	0·52	1·62	0·83	0·19
0·89	0·12	0·78	0·89	0·93	0·04	0·63	1·32	0·92	0·09
0·94	0·06	0·86	0·48	0·97	0·02	0·68	1·06		
0·98	0·02	0·90	0·32			0·73	0·92		
						0·79	0·65		
						0·88	0·34		
						0·94	0·22		

TABLE 4. *Adsorption from mixtures of piperidine and* cyclo*hexane on γ-alumina at* 20°.

Mole fraction of C_5H_{11} at equilibrium	0·02	0·06	0·11	0·16	0·20	0·25	0·36	0·49	0·57	0·67	0·81	0·88	0·95
$n_0\Delta x/m$ (mmoles/g.)	0·94	0·98	0·97	0·94	0·92	0·87	0·72	0·61	0·52	0·40	0·23	0·14	0·07

TABLE 5. *Adsorption from mixtures of* n-*butylamine and benzene; A, mole fraction of* Bu^nNH_2 *at equilibrium; B,* $n_0\Delta x/m$ *(mmoles/g.).*

A	*B*	*A*	*B*	*A*	*B*	*A*	*B*
Boehmite, 20°		Boehmite, 20°		Silica gel, 20°		γ-Alumina, 20°	
0·01	0·90	0·60	0·55	0·01	2·61	0·03	0·76
0·03	1·05	0·67	0·45	0·05	2·73	0·07	0·86
0·09	1·09	0·70	0·41	0·11	2·82	0·13	0·85
0·11	1·07	0·80	0·19	0·15	2·78	0·19	0·82
0·20	1·04	0·91	0·06	0·26	2·43	0·29	0·65
0·21	1·03	0·92	−0·05	0·35	2·20	0·38	0·60
0·36	0·84	0·95	−0·07	0·44	1·90	0·47	0·51
0·47	0·72	0·97	−0·05	0·56	1·43	0·58	0·36
				0·68	1·02	0·69	0·19
				0·77	0·76	0·79	0·11
				0·89	0·44	0·90	−0·02
						0·96	−0·03

TABLE 6. *Physical adsorption (mmoles/g.) from mixtures of pyridine and* cyclo*hexane at* 20°.

Mole fraction of C_5H_5N at equilibrium	C_5H_5N	C_6H_{12}	C_5H_5N	C_6H_{12}	Mole fraction of C_5H_5N at equilibrium	C_5H_5N	C_6H_{12}	C_5H_5N	C_6H_{12}
	on boehmite		on silica gel			on boehmite		on silica gel	
0·0	0·00	0·85	0·00	2·34	0·6	1·23	0·084	3·18	0·19
0·1	1·16	0·13	2·63	0·56	0·7	1·24	0·075	3·26	0·14
0·2	1·22	0·088	2·94	0·36	0·8	1·24	0·074	3·31	0·10
0·3	1·22	0·087	3·07	0·27	0·9	1·25	0·072	3·36	0·073
0·4	1·22	0·086	3·12	0·23	1·0	1·36	0·000	3·47	0·000
0·5	1·23	0·085	3·16	0·20					

TABLE 7. *Physical adsorption (mmoles/g.) from mixtures of piperidine and* cyclo*hexane at* 20°.

Mole fraction of $C_5H_{11}N$ at equilibrium	$C_5H_{11}N$	C_6H_{12}	$C_5H_{11}N$	C_6H_{12}	$C_5H_{11}N$	C_6H_{12}
	on boehmite		on silica gel		on γ-Al_2O_3	
0·0	0·00	0·86	0·00	2·36	0·00	0·50
0·1	0·75	0·25	1·22	1·36	0·38	0·22
0·2	0·79	0·22	1·38	1·23	0·47	0·18
0·3	0·81	0·21	1·55	1·08	0·50	0·13
0·4	0·81	0·21	1·72	0·96	0·54	0·10
0·5	0·82	0·20	1·91	0·80	0·55	0·09
0·6	0·82	0·20	2·07	0·66	0·57	0·08
0·7	0·84	0·19	2·29	0·50	0·59	0·07
0·8	0·86	0·17	2·47	0·34	0·62	0·04
0·9	0·90	0·13	2·68	0·18	0·64	0·03
1·0	1·07	0·00	2·89	0·00	0·68	0·00

TABLE 8. *Physical adsorption (mmoles/g.) from mixtures of* n-*butylamine and benzene at* 20°.

Mole fraction of Bu^nNH_2 at equilibrium	$BuNH_2$	C_6H_6	$BuNH_2$	C_6H_6	Mole fraction of Bu^nNH_2 at equilibrium	$BuNH_2$	C_6H_6	$BuNH_2$	C_6H_6
	on boehmite		on silica gel			on boehmite		on silica gel	
0·0	0·00	1·11	0·00	3·10	0·6	1·24	0·29	3·03	0·52
0·1	0·75	0·65	2·16	1·24	0·7	1·29	0·27	3·16	0·41
0·2	0·91	0·52	2·42	1·03	0·8	1·34	0·25	3·31	0·29
0·3	1·02	0·45	2·57	0·89	0·9	1·38	0·21	3·46	0·16
0·4	1·11	0·39	2·75	0·77	1·0	1·70	0·00	3·64	0·00
0·5	1·18	0·34	2·88	0·64					

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Discussion

Irreversible Adsorption.—The irreversible adsorption of the bases might be attributed to salt-formation by the bases with residual acid left in the solids. The smaller extent of the irreversible adsorption at 60° than at 20° makes this unlikely to be a complete explanation. For the same reason, the irreversible adsorption we have observed is not comparable with the adsorption of nitrogenous bases on the " acid centres " of alumina-silica cracking catalysts; [8] such adsorption is observed at about 300°. It is more nearly comparable with that observed by Khodadadi,[9] who found that for temperatures below 20° the total adsorption of ammonia on silica gel was either independent of, or increased with rise in, temperature depending on the type of gel used.

Regarding the surface sites responsible for this weak irreversible adsorption, it has been suggested that ammonia is held to a glass surface by hydrogen-bonding, the O–H···N bond being more likely than N–H···O.[10] Hydrogen-bonding may well be an important factor in the physical adsorption shown by the systems we have studied, but it does not explain the whole of the irreversible adsorption. There is considerable irreversible adsorption of pyridine by γ-Al_2O_3, a combination which does not possess the hydrogen atoms required for hydrogen-bonding. This system, moreover, appears to be no different from the others recorded, as far as irreversible adsorption is concerned.

It seems significant that we find no critical difference in adsorption on anhydrous alumina, boehmite, and " gibbsite "; approximately the same proportion of each surface is covered irreversibly by a given adsorbate. The specific rôle of the oxide ions in chemisorption of alcohols [1,2] is thus not repeated here. Similarly the difference in the amounts of pyridine held by the original and the " dehydrated " silica gel (the latter having a reduced number of hydroxide groups) is not significant.

The remaining site for chemisorption is the aluminium or silicon atom. This would involve the formation of a co-ordinate bond from the nitrogen atom of the base. Pyridine forms such a bond with the aluminium atom in aluminium chloride,[11] and ammine complexes with iron are very stable.[12] A similar bond to the chromium ion is suggested to account for chemisorption of water by chromia at room temperature.[13] On this assumption, the maximum amounts of chemisorption possible on boehmite have been calculated, by use of molecular areas of 24·7 Å^2 for pyridine (calculated from data of Pauling and Schomaker [14]) and 12·8 Å^2 for ammonia (calculated from density data and tables of bond lengths and angles). The results (Table 9) are equivalent to 2·40 mmoles/g. for ammonia

Table 9.

Plane	Area (Å^2)		No. of Al atoms		No. of Al atoms capable of reacting with NH_3		No. of Al atoms capable of reacting with C_5H_5N	
100	11·2	Total 39·1	1	Total 3	0·5	Total 2·0	0·25	Total 0·83
010	10·5		1		0·5		0·25	
001	17·4		1		1·0		0·33	

and 0·88 mmole/g. for pyridine, with an uncertainty similar to that discussed for chemisorption of alcohols.[1,2] The corresponding figures for γ-Al_2O_3 are 1·68 and 0·84 mmoles/g. respectively, which are much higher than those observed experimentally. Chemisorption clearly does not go to completion in this case. Together with the results for 60°, whereat

[8] Mills, Boedeker, and Oblad, *J. Amer. Chem. Soc.*, 1950, **72**, 1554.
[9] Khodadadi, *Compt. rend.*, 1957, **244**, 198.
[10] Yates, Sheppard, and Angell, *J. Chem. Phys.*, 1955, **23**, 1980.
[11] Muller, *Z. anorg. Chem.*, 1931, **156**, 70.
[12] Sidgwick, " The Chemical Elements and their Compounds," Clarendon Press, Oxford, 1950, p. 1361.
[13] Voltz and Weller, *J. Amer. Chem. Soc.*, 1953, **75**, 5231.
[14] Pauling and Schomaker, *ibid.*, 1939, **61**, 1769.

irreversible adsorption still occurs but to a smaller extent, this shows that the bases are held by much weaker forces than those responsible for chemisorption of the alcohols.

The relative strengths of the co-ordinate bonds as indicated by the extent of chemisorption of the three bases on each adsorbent increase in the order of the basic dissociation constants (Table 10):

TABLE 10.

Irreversible adsorption (mmoles/g.) on:	Pyridine $K = 2{\cdot}3 \times 10^{-9}$	*n*-Butylamine $K = 4{\cdot}2 \times 10^{-4}$	Piperidine $K = 1{\cdot}6 \times 10^{-3}$
Boehmite	0·44	0·52	0·65
Silica gel	0·96	1·12	1·38
γ-Al_2O_3	0·42	0·61	0·73

Thus the extent of co-ordination to the aluminium or silicon atom increases as the extent of co-ordination to the proton increases. Ammonia is not included in this comparison because its smaller molecular size allows it access to a higher proportion of each surface than is available to the organic bases.

Adsorption from the Liquid Phase.—In adsorption from the liquid phase, the total process can be regarded as competitive physical adsorption, confined to one layer of physically adsorbed molecules, on a surface partially covered by irreversibly adsorbed base. The bases are physically adsorbed to a much greater extent than the indifferent hydrocarbons. The mole fraction of pyridine in the adsorbed phase on each adsorbent is greater than that of the other two bases, possibly partly because of its more polar character, but it may also be significant, as we observed elsewhere,[15] that the least volatile of otherwise similar substances is the most strongly adsorbed.

EXPERIMENTAL

Adsorbents.—The adsorbents were those described previously.[1, 2]

Adsorbates.—*n*-Butylamine was stored over sodium wire until evolution of hydrogen ceased, and fractionally distilled. It had n_D^{20} 1·4007 (cf. 1·4009 given by Vogel [16]). Piperidine was stored over solid potassium hydroxide and fractionally distilled. It had n_D^{20} 1·4528 (cf. 1·4533 given by Fowler [17]). Ammonia from a cylinder was dried by passing it over alumina and then over glass wool impregnated with sodium; the sodium was deposited by soaking the glass wool in a solution of sodium in liquid ammonia and evaporating off the ammonia. The purification of the other adsorbates has been described.[18]

Monolayer (BET) values for physical adsorption on the solids, following chemisorption of the respective base, are given in Figs. 2 and 3 and Tables 6—8, referred to 1 g. of the original solid.

Procedure.—Desorption experiments were carried out according to method A of our previous paper.[2] Liquid-phase adsorption was carried out at 20° by previous methods. As the "irreversible" adsorption was established rapidly for these systems, one day's contact only was allowed between adsorbent and adsorbate in the liquid-phase experiments. Table 11 shows that this procedure was satisfactory.

TABLE 11. *Adsorption on boehmite at 20° from a mixture of pyridine and* cyclo*hexane (equilibrium mole fraction of pyridine* = 0·215).

Time of shaking	1 hr.	2 hr.	4 hr.	8 hr.	1 day	3 days	7 days	14 days	27 days
$n_o\Delta x/m$ (mmoles/g.) *	1·18	1·23	1·28	1·26	1·27	1·27	1·27	1·27	1·26

* Mean of two values in each case.

THE UNIVERSITY, HULL. [*Received, August 8th,* 1957.]

[15] Blackburn, Kipling, and Tester, *J.*, 1957, 2373.
[16] Vogel, *J.*, 1948, 1825.
[17] Fowler, *J. Appl. Chem.*, 1951, **1**, 848.
[18] Blackburn and Kipling, *J.*, 1954, 3819.

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40. *Chemical Reactions with Vanadium, Niobium, and Tantalum Pentafluorides.*

By H. C. Clark and H. J. Emeléus.

Vanadium pentafluoride reacted with nitryl fluoride and nitrosyl fluoride to form nitronium and nitrosonium hexafluorovanadates. The corresponding hexafluoroniobates and hexafluorotantalates were best prepared from the metal oxide, bromine trifluoride, and dinitrogen tetroxide or nitrosyl chloride. Chloryl hexafluorovanadate was stable only at low temperatures. Dissociation pressures of nitronium and nitrosonium hexafluorovanadates and of nitrosonium hexafluoroniobate were measured. The reactions of the pentafluorides with sulphur dioxide and trioxide and of niobium and tantalum pentafluorides with pyridine were studied.

The reactive molybdenum hexafluoride and vanadium pentafluoride can be satisfactorily examined [1,2] in glass apparatus free from moisture and vacuum grease. The physical properties of vanadium pentafluoride led to the suggestion that it ionises in the liquid state: $2VF_5 \rightleftharpoons VF_4^+ + VF_6^-$. Fairbrother, Frith, and Woolf [3] suggested, as a result of conductivity measurements, that a similar self-ionisation also occurs in molten niobium and tantalum pentafluorides. For all three pentafluorides the physical evidence for self-ionisation is provided by the high values of Trouton's constant and the appreciable electrical conductivities. Supporting indirect chemical evidence is found in the isolation of hexafluoro-vanadates,[4] -niobates,[5] and -tantalates [5] which contain the MF_6^- ions. The influence of such self-ionisation on the chemical properties of these pentafluorides has now been examined by a study of their reactions, mainly with oxides and other fluorides.

Although the hexafluorovanadates are known, no compound containing the " acidic " VF_4^+ ion has been isolated. The formulation [6] of the product of the reaction of iodine pentafluoride with antimony pentafluoride as $IF_4^+SbF_6^-$ suggests that a similar reaction with vanadium pentafluoride might give $VF_4^+SbF_6^-$. However, no such compound was isolated, although it may have been present in a solution of antimony pentafluoride in vanadium pentafluoride. The addition of potassium fluoride to this solution, followed by the removal of all volatile materials, left potassium hexafluoroantimonate. This can be explained in terms of either a simple neutralisation (*a*) or an addition reaction (*b*):

$$K^+VF_6^- + VF_4^+SbF_6^- \rightleftharpoons KSbF_6 + 2VF_5 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (a)$$

$$K^+ + F^- + SbF_5 = KSbF_6 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (b)$$

Similarly, the reactions of vanadium or niobium pentafluoride with boron trifluoride should produce $MF_4^+BF_4^-$ derivatives, but these reactions appeared not to give stable products. This is not surprising since the corresponding derivative of bromine trifluoride, $BrF_2^+BF_4^-$, has not yet been isolated.

To illustrate the formation of the hexafluoro-salts, the reactions of some of these pentafluorides with nitryl, nitrosyl, and chloryl fluorides were studied. With nitryl fluoride, vanadium pentafluoride forms involatile, white nitronium hexafluorovanadate, NO_2VF_6. Previous attempts [7] to produce this compound by the action of bromine trifluoride on mixtures of dinitrogen tetroxide and vanadium trichloride gave products intermediate in composition between the tetrafluoro-oxyvanadate and the hexafluorovanadate. Niobium pentafluoride did not react completely with nitryl fluoride at room

[1] O'Donnell, *J.*, 1956, 4681.
[2] Clark and Emeléus, *J.*, 1957, 2119.
[3] Fairbrother, Frith, and Woolf, *J.*, 1954, 1031.
[4] Emeléus and Gutmann, *J.*, 1949, 2979.
[5] Gutmann and Emeléus, *J.*, 1950, 1046.
[6] Woolf, *J.*, 1950, 3678.
[7] Sharpe and Woolf, *J.*, 1951, 798.

temperature, probably because of the formation of a protective coating of hexafluoroniobate. The nitronium salt is best prepared by the action of bromine trifluoride on dinitrogen tetroxide and niobium pentoxide. Nitronium hexafluoroniobate is a white solid from which all traces of bromine trifluoride cannot be satisfactorily removed. Similar treatment of tantalum pentoxide with dinitrogen tetroxide and bromine trifluoride gives only partial conversion into nitronium hexafluorotantalate and the pure salt could not be isolated.

Nitrosyl fluoride reacts rapidly with vanadium pentafluoride to form nitrosonium hexafluorovanadate, $NOVF_6$. This had been prepared [7] by bromine trifluoride treatment of nitrosyl chloride and vanadium trichloride. Nitrosonium hexafluoro-niobate and -tantalate, $NONbF_6$ and $NOTaF_6$, have now been prepared by treatment with bromine trifluoride of mixtures of nitrosyl chloride with niobium or tantalum pentoxide. Both are white solids which dissolve readily in water and from which all traces of bromine trifluoride cannot be removed. At the temperatures required for complete removal, decomposition is appreciable. The retention of bromine trifluoride may be attributed to solvolysis, *e.g.*, $NONbF_6 + 2BrF_3 \longrightarrow NOBrF_4 + BrF_2,NbF_6$, which occurs with the calcium and barium hexafluoro-niobates and -tantalates.[5]

The direct reaction of chloryl fluoride with other fluorides has led [8,9] to the isolation of the compounds ClO_2F,BF_3, ClO_2F,PF_5, and ClO_2F,SbF_5 which can be formulated as the "chloronium" salts $ClO_2^+BF_4^-$, $ClO_2^+PF_6^-$, and $ClO_2^+SbF_6^-$. With tantalum pentafluoride, chloryl fluoride gives a product containing only 0·48 mole of chloryl fluoride per mole of pentafluoride. Woolf attributed this to the slowness of the reaction at room temperature. Chloryl fluoride has now been allowed to react with vanadium pentafluoride. The reaction products were unstable at room temperature and experiments were made to isolate them at −46° and −78°. They were white solids which decomposed at higher temperatures to the original reactants. The product obtained at −46° contained 0·63 mole of chloryl fluoride per mole of pentafluoride while for the product of isolation at −78° the ratio was 0·97 : 1. This "chloronium hexafluorovanadate" is stable only at low temperatures and probably the low ratio observed by Woolf for the reaction with tantalum pentafluoride is due, not to the slowness of the reaction, but to the instability of the salt at ordinary temperatures. Further information on stability has been obtained from measurements of the dissociation pressures of nitronium and nitrosonium hexafluorovanadates and nitrosonium hexafluoroniobate. From these measurements, the following values have been calculated, simple dissociation being assumed to occur, *e.g.*, $NO_2VF_6(s) \longrightarrow NO_2F(g) + VF_5(g)$:

	ΔH (kcal./mole)	ΔG (50°) (kcal./mole)	ΔS (50°) (cal./deg./mole)
NO_2VF_6	13·75	6·15	23·5
$NOVF_6$	18·00	3·47	35·7
$NONbF_6$	20·5	4·84	48·6

From a consideration of the energetics of these dissociation processes for nitronium and nitrosonium hexafluorovanadates, three terms can be seen to differ; namely, the dissociation energies of nitryl and nitrosyl fluorides, the ionisation energies of the nitronium and nitrosonium ions, and the lattice energies of the original hexafluorovanadates. The difference in the dissociation energies is not likely to be large since in both cases dissociation involves the breaking of a nitrogen–fluorine bond. The other two energy differences will therefore determine the difference in stability, although the two factors cannot be readily separated. These results, together with the observed instability of chloronium hexafluorovanadate, indicate that the order of stability is $NO^+ > NO_2^+ > ClO_2^+$. Nitrosonium hexafluoroniobate is also seen to be more stable than the corresponding hexafluorovanadate. This difference in stability will again be related to the different radii of the VF_6^- and NbF_6^- ions, and to the relative energies of the reaction $MF_6^- \longrightarrow MF_5 + F^-$.

[8] Woolf, *J.*, 1954, 4113.
[9] Schmeisser and Ebenhoch, *Angew. Chem.*, 1954, **66**, 230.

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Measurements of the dissociation pressures of nitronium hexafluoroniobate and nitrosonium hexafluorotantalate were not made, as it was not possible to prepare these salts free from bromine trifluoride.

With excess of sulphur dioxide, vanadium pentafluoride reacts quantitatively to form thionyl fluoride and vanadium oxytrifluoride:

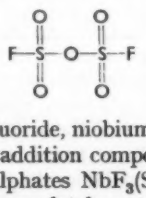
$$VF_5 + SO_2 \longrightarrow VOF_3 + SOF_2$$

Niobuim pentafluoride does not react at room temperature with sulphur dioxide. This difference between the two pentafluorides may be due to their different degrees of self-ionisation. Since excess of liquid sulphur dioxide was employed in both reactions, it seems reasonable to relate the mechanism of the reaction to that of the sulphur dioxide solvent system. The reaction with vanadium pentafluoride may therefore involve, as reaction intermediates, unstable complexes of the type $SO(VF_6)_2$ and $(VF_4)_2SO_3$. Similar complexes of niobium pentafluoride may not be formed so readily. Iodine pentafluoride, whose specific conductivity is of the same order as that of niobium pentafluoride, also does not react with sulphur dioxide.[10]

At room temperature, vanadium pentafluoride reacts readily with sulphur trioxide to form pyrosulphuryl fluoride and vanadium oxytrifluoride, $VF_5 + 2SO_3 \longrightarrow VOF_3 + S_2O_5F_2$. Pyrosulphuryl fluoride boils at 51°, in agreement with Hayek and Koller's value,[11] the latent heat of vaporisation is 7600 cal. mole^{-1} and the Trouton constant 23·5. Scheurer and Le Fave [12] suggested a structure of pyrosulphuryl fluoride involving S–O–F groups, but this seems unlikely since the analogous pyrosulphuryl chloride has [13] the chlorine atoms linked directly to sulphur. The infrared absorption spectrum of pyrosulphuryl fluoride shows that it has S–F and not S–O–F groups as can be seen from the comparison of the principal absorption bands of several sulphur oxyfluorides shown in the Table.

Assignment	Sulphuryl fluoride [14] SO_2F_2	Fluorine fluorosulphate [15] SO_3F_2	Peroxydisulphuryl fluoride [16] $S_2O_6F_2$	Pyrosulphuryl fluoride $S_2O_5F_2$
S–O stretching	1502	1501	1495	1513
	1269	1248	1246	1248
S–F stretching (asymmetric and symmetric)	885	879	—	872
	848	852	848	824
S–O stretching of S–O–F group	—	789	—	—
Unassigned	767	—	755	735

The structure of pyrosulphuryl fluoride therefore appears to be



As distinct from vanadium pentafluoride, niobium and tantalum pentafluorides reacted with sulphur trioxide to produce the addition compounds $NbF_5,2{\cdot}1SO_3$ and $TaF_5,2{\cdot}6SO_3$, which can be formulated as fluorosulphates $NbF_3(SO_3F)_2$ and $TaF_3(SO_3F)_2$ from which excess of sulphur trioxide has been incompletely removed. These compounds are viscous liquids which fume and decompose on exposure to air, and smell slightly of pyrosulphuryl fluoride. From both the niobium and tantalum compounds, thermal decomposition at 175—225° produced sulphuryl fluoride. Their formulation as fluorosulphates follows from a comparison with other fluorosulphates and with the reactions of other fluorides

[10] Aynsley, Nichols, and Robinson, *J.*, 1953, 623.
[11] Hayek and Koller, *Monatsh.*, 1951, **82**, 942.
[12] Scheurer and Le Fave, Abs. 118th Meeting, Amer. Chem. Soc., 1950, 26L.
[13] Gerding and Linden, *Rec. Trav. chim.*, 1942, **61**, 735.
[14] Perkins and Wilson, *J. Chem. Phys.*, 1952, **20**, 1791.
[15] Dudley, Cady, and Eggers, *J. Amer. Chem. Soc.*, 1956, **78**, 290.
[16] Dudley and Cady, *J. Amer. Chem. Soc.*, 1957, **79**, 513.

with sulphur trioxide. Thus, bromine trifluoride and sulphur trioxide form the product $BrF_3,1{\cdot}37SO_3$, a rather viscous liquid which can be formulated as $BrF_2^+SO_3F^-$. All the reactions of this compound show it to be a fluorosulphate.[17] Again, tantalum pentachloride reacts with fluorosulphuric acid [18] to give the fluorosulphate $TaCl_3(SO_3F)_2$. Using niobium pentachloride we obtained an unidentified viscous material and this probably has the formula $NbCl_3(SO_3F)_2$. There is a close resemblance between these compounds and the above pentafluoride derivatives. Finally, the infrared absorption spectrum of the niobium pentafluoride–sulphur trioxide compound, although not well resolved, showed definite bands at frequencies of 767 cm.$^{-1}$ and 1057 cm.$^{-1}$. These bands have been recently assigned to the S–F and to the S–O stretching frequencies respectively of the fluorosulphate group.[19,20] The reactions of the pentafluorides of niobium and tantalum with sulphur trioxide therefore take place through the formation of fluorosulphates:

$$MF_5 + 2SO_3 \longrightarrow MF_3(SO_3F)_2 \longrightarrow MOF_3 + S_2O_5F_2$$

The fluorosulphate derivative of vanadium pentafluoride is evidently unstable and the reaction proceeds to completion. With niobium and tantalum pentafluorides, the fluorosulphates are the stable products. It is not clear why thermal decomposition of the latter should produce sulphuryl rather than pyrosulphuryl fluoride.[21]

The new compounds dipyridinepentafluoroniobium(v), $(C_5H_5N)_2NbF_5$, and dipyridinepentafluorotantalum(v), $(C_5H_5N)_2TaF_5$, have been prepared by the direct reaction of pyridine with each of the pentafluorides. Both compounds are white solids which are stable in air and dissolve readily in water. Attempts were made to convert these pyridine compounds into pyridinium salts by treatment with concentrated aqueous hydrofluoric acid. The pyridinium fluorotantalates $(C_5H_5NH)_3TaF_8,2H_2O$ and $(C_5H_5NH)TaF_6$ have been prepared by Balke.[22] In the present case, repeated treatment of the dipyridine niobium compound with aqueous hydrofluoric acid gave pyridinium hexafluoroniobate, $(C_5H_5NH)NbF_6$, while similar treatment of the tantalum compound gave a product intermediate in composition between pyridinium hexafluorotantalate and dipyridinium heptafluorotantalate. This seems a further instance of the greater stability of the septavalent state of tantalum than of niobium.

Experimental

The preparation and analysis of vanadium pentafluoride have been described.[3] Niobium and tantalum pentafluorides were prepared by direct fluorination of the powdered metals at 350°. Niobium and tantalum were estimated in solutions of the pentafluorides by precipitation with ammonium hydroxide followed by ignition to the pentoxides. Fluorine was determined by precipitation as calcium fluoride (Found: Nb, 49·3; F, 50·4. Calc. for NbF_5: Nb, 49·4; F, 50·6. Found: Ta, 65·3; F, 34·3. Calc. for TaF_5: Ta, 65·6; F, 34·4%).

All reactions were carried out in high-vacuum systems in which the conventional taps and joints were replaced by grease-free capillaries and break-seals. The volatile products of each reaction were separated and purified by fractionation in similar systems and the various fractions were identified by vapour pressures and molecular weights by use of the apparatus previously described.[1] Involatile residues were analysed for vanadium, niobium, or tantalum and fluorine by the above methods. Infrared absorption spectra were determined with a Perkin-Elmer Model 21 double-beam recording spectrophotometer with a sodium chloride optical system.

Reaction with Antimony Pentafluoride.—Antimony pentafluoride, prepared by direct fluorination of the trioxide, gave no visible reaction with excess of vanadium pentafluoride. Fractionation of the liquid mixture gave incomplete separation of the reactants and left no residue.

[17] Woolf, *J.*, 1950, 1053.
[18] Hayek, Puschmann, and Czaloun, *Monatsh.*, 1954, **85**, 359.
[19] Siebert, *Z. anorg. Chem.*, 1957, **289**, 15.
[20] Sharp, *J.*, 1957, in the press.
[21] Hayek, Czaloun, and Krismer, *Monatsh.*, 1956, **87**, 741.
[22] Balke, *J. Amer. Chem. Soc.*, 1905, **27**, 1140.

Addition of dry potassium fluoride to the mixture, followed by the removal of all volatile material, left white potassium hexafluoroantimonate (Found: Sb, 45·9; F, 43·6. Calc. for $KSbF_6$: Sb, 46·0; F, 43·1%).

Reactions with Boron Trifluoride.—Pure boron trifluoride was kept with vanadium pentafluoride at −78° in a sealed apparatus for 20 hr. The volatile products were then separated into fractions condensing at −78° and −184°. The −78° fraction was unchanged vanadium pentafluoride and the −184° fraction boron trifluoride (Found: *M*, 68·5. Calc. for BF_3: *M*, 67·8). The least volatile portion of the reaction mixture was analysed for vanadium (Found: V, 35·6. Calc. for VF_5: V, 34·9%). Similarly, niobium pentafluoride did not react with boron trifluoride since the final portion of the reaction mixture was unchanged niobium pentafluoride (Found: Nb, 49·5. Calc. for NbF_5: Nb, 49·4%).

Reactions with Nitryl Fluoride.—Nitryl fluoride, prepared by direct fluorination of sodium nitrite,[23] reacted rapidly with vanadium pentafluoride at −78° to give an involatile white solid identified as *nitronium hexafluorovanadate* (Found: V, 24·5; F, 53·5. NO_2VF_6 requires V, 24·2; F, 54·1%). This compound was hygroscopic and dissolved instantly in water. A similar reaction of nitryl fluoride with niobium pentafluoride gave very incomplete conversion into nitronium hexafluoroniobate (Found: Nb, 47·8. NO_2NbF_6 requires Nb, 36·7. Calc. for NbF_5: Nb, 49·4%).

Reaction with Nitrosyl Fluoride.—Nitrosyl fluoride was prepared by the direct union of nitric oxide and fluorine carried in a stream of nitrogen in a silica tube, and was made to react immediately in an all-glass apparatus with vanadium pentafluoride. The product was white. involatile nitrosonium hexafluorovanadate, $NOVF_6$ (Found: V, 26·6. Calc. for $NOVF_6$: V, 26·2%).

Preparation of Hexafluoro-niobates and -tantalates with Bromine Trifluoride.—The methods of Woolf and Emeléus [24] were employed. Bromine trifluoride reacted with niobium pentoxide and dinitrogen tetroxide to give *nitronium hexafluoroniobate*, NO_2NbF_6 (Found: Nb, 35·6; F, 45·5. NO_2NbF_6 requires Nb, 36·6; F, 45·1%), a white solid, readily soluble in water and decomposing above *ca.* 60°. Similar treatment with bromine trifluoride of a mixture of niobium pentoxide and nitrosyl chloride gave *nitrosonium hexafluoroniobate*, $NONbF_6$ (Found: Nb, 38·1. $NONbF_6$ requires Nb, 39·2%), a white solid, soluble in water and decomposing above 60—70°. Bromine trifluoride with tantalum pentoxide and dinitrogen tetroxide gave only partial conversion into nitronium hexafluorotantalate, despite vigorous boiling (Found: Ta, 56·5. Calc. for NO_2TaF_6: Ta, 53·1%). However with nitrosyl chloride and tantalum pentoxide, *nitrosonium hexafluorotantalate*, $NOTaF_6$, was formed (Found: equiv., 336; Ta, 54·0. $NOTaF_6$ requires equiv., 325; Ta, 55·7%) as a soluble white solid. All these nitronium and nitrosonium hexafluoro-niobates and -tantalates gave low analytical results for niobium and tantalum, owing to the presence of bromine trifluoride. This could only be completely removed by heating to at least 60°, at which temperature the compounds decomposed.

The dissociation pressures of these salts were measured in the range 25—95° with a modification of the all-glass apparatus previously described for the measurement of the vapour pressure of vanadium pentafluoride. All transfers of the salts were performed in a "dry-box." For nitronium hexafluorovanadate, nitrosonium hexafluorovanadate, and nitrosonium hexafluoroniobate, $\log_{10} p(\text{mm.}) = 9{\cdot}726 - 2725/T$, $13{\cdot}45 - 4048/T$, and $15{\cdot}71 - 4580/T$ respectively.

Reaction with Chloryl Fluoride.—Chloryl fluoride was prepared by Woolf's method,[8] by the reaction of bromine trifluoride with potassium chlorate. As the fluoride thus prepared in glass apparatus is highly reactive and rather impure, its molecular weight could not be determined. Its reactivity with glass was shown by the rapid intensification of the red colour on exposure to glass surfaces at room temperature. In the first preparation, chloryl fluoride was allowed to react immediately with vanadium pentafluoride at −46°. After standing for some hours to ensure completion of the reaction, all substances volatile at −46° were distilled off leaving a white solid which, on warming to room temperature, appeared to decompose. This solid had a V : Cl ratio of 1 : 0·63. The second reaction was performed at −78° and an unstable white solid was obtained which contained vanadium and chlorine in the ratio 1 : 0·97.

Reactions with Sulphur Dioxide.—Excess of dry sulphur dioxide was distilled in a grease- and moisture-free apparatus onto vanadium pentafluoride. There was a vigorous reaction. The

[23] Aynsley, Hetherington, and Robinson, *J.*, 1954, 1119.
[24] Woolf and Emeléus, *J.*, 1950, 1050, 1053.

volatile products were separated into fractions condensing at −132° and −120°, and there remained a pale yellow involatile residue. The −132° fraction (1·66 g.) was thionyl fluoride (Found: *M*, 87·6; b. p. −47°. Calc. for SOF_2: *M*, 86; lit. b. p. −44°). The −120° fraction was sulphur dioxide (Found: *M*, 64·6. Calc. for SO_2: *M*, 64·0). The involatile residue was hygroscopic, dissolved instantly in water, and was vanadium oxytrifluoride (Found: V, 41·1; F, 44·6. Calc. for VOF_3: V, 41·1; F, 46·0%). By estimating from the total amount of vanadium present, the weight of vanadium pentafluoride used in the reaction, the yield of thionyl fluoride was found to be 97·8%.

The reaction of sulphur dioxide with niobium pentafluoride was examined similarly. In this case the only volatile fraction condensed at −120° and was unchanged sulphur dioxide (Found: *M*, 64·7. Calc. for SO_2: *M*, 64·0). The remaining solid was unchanged pentafluoride (Found: Nb, 49·1. Calc. for NbF_5: Nb, 49·4%).

Reactions with Sulphur Trioxide.—Pure, dry sulphur trioxide, prepared from fuming sulphuric acid and phosphoric oxide, reacted readily at room temperature with vanadium pentafluoride to give volatile products condensing at −78° and −46°. A pale yellow involatile hygroscopic solid remained and this was vanadium oxytrifluoride (Found: ratio V : F, 1 : 3·02. Calc. for VOF_3: V : F, 1 : 3·00). The compound which condensed as a white solid at −78° and melted at approximately −50° to a clear liquid was pyrosulphuryl fluoride (Found: *M*, 183. Calc. for $S_2O_5F_2$: *M*, 182·0). Vapour-pressure measurements over the temperature range −28° to 43° gave $\log_{10} p(\text{mm.}) = 8{\cdot}015 - 1662/T$. The −46° fraction was a small excess of vanadium pentafluoride.

The reactions of niobium and tantalum pentafluorides with sulphur trioxide proceeded more slowly, producing in both cases, after several hours, clear viscous liquids. By heating them *in vacuo* to 50° for 2 hr., excess of sulphur trioxide and other volatile materials were removed, the viscous compounds being almost involatile. The negligible volatile fractions were mainly sulphur trioxide together with some less volatile material, but no satisfactory separation was achieved. In the reaction with niobium pentafluoride, a trace of pyrosulphuryl fluoride was also liberated (Found: *M*, 175. Calc. for $S_2O_5F_2$: *M*, 182). Both viscous products fumed in air, reacted vigorously with water, and had a strong odour of pyrosulphuryl fluoride. Analyses of their solutions identified the compounds as NbF_5,2·1SO_3 (Found: Nb, 25·8; SO_3, 47·7. NbF_5,2·1SO_3 requires Nb, 25·7; SO_3, 47·3%) and TaF_5,2·6SO_3 (Found: Ta, 37·5; SO_3, 43·1. TaF_5,2·6SO_3 requires Ta, 37·4; SO_3, 43·0%). Thermal decomposition at 172° in a sealed tube for 24 hr. produced sulphuryl fluoride (Found: *M*, 102. Calc. for SO_2F_2: *M*, 102). The tantalum compound decomposed at 225°, also producing sulphuryl fluoride (Found: *M*, 103). Measurement of the infrared absorption spectrum of the niobium compound NbF_5,2·1SO_3 was difficult as the high viscosity and ease of hydrolysis prevented preparation of a sufficiently thin film. The spectrum was therefore not well resolved.

Reactions with Pyridine.—Niobium and tantalum pentafluorides reacted rapidly with dry pyridine to produce white solids which were quite stable to air and dissolved quietly in water. Analyses of their solutions identified the solids as *dipyridinepentafluoroniobium*(v) (Found: Nb, 27·7; F, 27·7. $(C_5H_5N)_2NbF_5$ requires Nb, 26·9; F, 27·5%) and *dipyridinepentafluorotantalum*(v) [Found: Ta, 41·0; F, 22·0. $(C_5H_5N)_2TaF_5$ requires Ta, 41·7; F, 21·8%]. Both compounds decomposed without melting when heated to 100°. Treatment of the niobium compound with concentrated aqueous hydrofluoric acid gave *pyridinium hexafluoroniobate* [Found: Nb, 32·1; F, 40·3. $(C_5H_5NH)NbF_6$ requires Nb, 32·2; F, 39·8%]. Similar repeated treatment of the tantalum compound gave a product intermediate in composition between pyridinium hexafluorotantalate and dipyridinium heptafluorotantalate [Found: Ta, 42·4; F, 29·0. Calc. for $(C_5H_5NH)TaF_6$: Ta, 48·2; F, 30·4. Calc. for $(C_5H_5NH)_2TaF_7$: Ta, 38·2; F, 28·1%]. Further treatment with hydrofluoric acid did not alter the composition.

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41. *The Thorium Dioxide–Thorium Tetrafluoride System.*

By R. W. M. D'Eye.

The thorium dioxide–thorium tetrafluoride system has been studied by *X*-ray diffraction. Thorium tetrafluoride dissolves in thoria to the extent of about 25 moles %, the cell constant *a* increasing from 5·586 to 5·663 *kX*. The arrangement of the anions in these mixed crystals is discussed. No solid solubility of thoria in thorium tetrafluoride was observed. Thorium oxyfluoride, $ThOF_2$, was formed by the reaction of equimolar mixtures of thoria and the tetrafluoride at 900° in an inert atmosphere. Diffraction photographs showed that the true unit cell of the oxyfluoride is orthorhombic and not hexagonal as previously suggested. The deviation from hexagonal symmetry is probably due to the oxygen and fluorine atoms' segregating into distinct sets of lattice sites. Attempts to prepare disordered thorium oxyfluoride with a random anion distribution were unsuccessful.

X-Ray powder diffraction and density studies of anomalous mixed-crystal systems such as CaF_2–YF_3,[1,2,3] CaF_2–ThF_4,[3] BaF_2–UF_3,[4] and BaF_2–UF_4 [5] have shown that, in the fluorite mixed-crystal phase, the cations are randomly distributed over the normal cation sites of the fluorite-type lattice (the positions 000 etc.), and the extra anions needed for electric neutrality occupy, presumably statistically, the largest " holes " in the lattice (the positions $\frac{1}{2}00$ etc.). Alberman and Anderson,[6] in discussing the effect of interstitial anions on a fluorite-type lattice, suggest that the net effect on the cell dimensions is determined by the interplay of the size and charge of the substituting cation with the distortion caused by the interstitial anion. Thus, if the radii of the cations are similar, the lattice-distortion effect will probably predominate, causing the cell to expand as the anion–cation ratio increases. This is true for the systems CaF_2–YF_3,[3] SrF_2–LaF_3,[3,7] and CaF_2–ThF_4.[3] If, however, the substituting cation is smaller as well as more highly charged, these effects may outweigh the distortion effect of the interstitial anions so that the cell contracts as the anion–cation ratio increases, as in the systems BaF_2–UF_3,[4] SrF_2–UF_3, and BaF_2–UF_4.[5]

These considerations also apply to certain oxide systems [8,9,10] and, as now shown, oxide–fluoride systems having the fluorite-type structure.

Zachariasen [11] found that in the La_2O_3–LaF_3 system lanthanum oxyfluoride, LaOF, can exist in two forms; when the composition corresponds exactly to LaOF the structure is rhombohedral, and when there is an excess of lanthanum trifluoride the structure is tetragonal. Both structures are based on a fluorite-type lattice. The deviation from cubic symmetry is due to the segregation of oxygen and fluorine atoms into distinct sets of lattice sites.

The present work gives evidence for the existence of a fluorite-type mixed crystal containing randomly distributed oxygen and fluorine atoms. In these mixed crystals there are two possible anionic arrangements: (i) the normal anion positions $\frac{1}{4}\frac{1}{4}\frac{1}{4}$, etc., in the unit cell are all occupied and the interstitial positions $\frac{1}{2}00$, etc., are statistically filled or (ii) both sets of lattice sites are statistically occupied. However, the difference in the calculated intensities is so small that it is not possible to distinguish between them.

[1] Vogt, *Neues Jahrb. Mineral.*, 1914, **2**, 9.
[2] Goldschmidt, *Geochem. Verteilungsgesetze*, 1926, **7**, 88.
[3] Zintl and Udgård, *Z. anorg. Chem.*, 1939, **240**, 150.
[4] D'Eye and Martin, *J.*, 1957, 1847.
[5] D'Eye and Ferguson, unpublished work.
[6] Alberman and Anderson, *J.*, 1949, S305.
[7] Ketelaar and Willems, *Rec. Trav. chim.*, 1937, **56**, 29.
[8] Hering and Perio, *Bull. Soc. chim. France*, 1952, **19**, 351.
[9] Rundle, Baenziger, and Wilson, 1947, MDDC-1608 (American Atomic Energy Report).
[10] Gronvold, *J. Inorg. Nuclear Chem.*, 1955, **1**, 257.
[11] Zachariasen, *Acta Cryst.*, 1951, **4**, 231.

Solid Solubility Limits.—The results of previous [1,2] work on systems such as CaF_2–ThF_4 [3] and BaF_2–UF_3 [4] show that at the limit of solid solubility there are two interstitial anions per unit cell. Thus, in the present system, the solid solubility limit of thorium tetrafluoride in thoria should be 25 moles %. We have been unable to confirm this figure owing to the difficulty of preparing homogeneous mixed-crystals phases. We found no solid solubility of thoria in thorium tetrafluoride.

Thorium Oxyfluoride.—Zachariasen [12] found from *X*-ray powder data that thorium oxyfluoride had a bimolecular hexagonal unit cell with $a = 4{\cdot}039 \pm 0{\cdot}002$ *kX* and $c = 7{\cdot}290 \pm 0{\cdot}004$ *kX*. As the structure was supposed to be of the LaF_3-type an alternative hexagonal unit cell was suggested [13] which contained six molecular units of $ThOF_2$ and had the dimensions $a = 4{\cdot}039\sqrt{3}$ and $c = 7{\cdot}290$ *kX*. Both structures require a random distribution of the oxygen and fluorine atoms over the anion positions in the lattice.

We now find that thorium oxyfluoride has an orthorhombic unit cell, the dimensions being closely related to those of the bimolecular hexagonal cell by the expressions $a_O \sim 2\sqrt{3}a_H$, $b_O \sim a_H$, $c_O \sim c_H$, where the subscripts O and H denote orthorhombic and hexagonal symmetry respectively. We suggest that the deviation from hexagonal symmetry is due to the ordering of the oxygen and fluorine atoms. All our attempts to prepare disordered thorium oxyfluoride, which would give diffraction photographs with no superlattice lines, were unsuccessful.

Experimental

Thorium Dioxide.—Thoria of small particle size was prepared by thermal decomposition of thorium oxalate [14] at 450° in air.

Thorium Tetrafluoride.—Thorium tetrafluoride of small particle size was prepared by the thermal degradation of the hydrate, ThF_4,yH_2O, [15, 16, 17] at 400° *in vacuo* or in an inert atmosphere.

Mixed Crystals.—Most samples were prepared by heating intimate mixtures of the tetrafluoride and thoria, in the requisite quantities, either (i) in platinum boats in argon which was purified by passage through traps cooled in liquid oxygen and then over heated copper turnings or (ii) *in vacuo* in sealed platinum bombs. In the latter method the sample was placed in a 4 mm. diameter platinum tube, sealed at one end. The open end was connected through glass tubing to a vacuum system. The apparatus was evacuated and the sample outgassed at 200°. When cool, the platinum tube was crimped about 1 in. above the level of the sample and an oxy–coal gas flame was played across the crimped portion. The platinum bomb was then sealed inside an evacuated quartz bomb.

Samples were generally heated at about 1000° for 6 hr. The thoria-rich mixed crystals could not be melted owing to their high m. p. (m. p. of thoria is *ca.* 3000°). These preparations were therefore never homogeneous.

Zachariasen [11] prepared samples in the range MF_3—M_2O_3, where M is lanthanum or yttrium, by heating the trifluoride at 900° in an atmosphere of low humidity. Hydrolysis proceeds until the fluoride is completely converted into oxide. We similarly prepared samples by heating thorium tetrafluoride in air at 440° in open platinum dishes; this temperature gave a convenient rate of hydrolysis. However, at the thoria-rich end of the system the samples were again never homogeneous.

Chemical Analysis.—The fluorine in the sample was estimated by the pyrohydrolytic method.[18] Steam was passed over the sample in a platinum boat, which was heated to 900—1000°. The resulting hydrofluoric acid–water mixture was condensed and titrated with

[12] Zachariasen, *Acta Cryst.*, 1949, **2**, 388.
[13] Oftedal, *Z. phys. Chem.*, 1931, *B*, **13**, 190.
[14] D'Eye and Sellman, *J. Inorg. Nuclear Chem.*, 1955, **1**, 143.
[15] D'Eye and Booth, *J. Inorg. Nuclear Chem.*, 1955, **1**, 326.
[16] D'Eye, Booth, and Harper, U.K.A.E.A. Report A.E.R.E. C/R 1735 (1955).
[17] D'Eye and Booth, *J. Inorg. Nuclear Chem.*, 1957, **4**, 13.
[18] Gillies, Keen, Lister, and Rees, U.K.A.E.A. Report A.E.R.E. C/M 225 (1954).

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standard alkali. The steam jet was then removed and the residual oxide ignited in air and weighed as thorium dioxide.

X-*Ray Diffraction.*—For the *X*-ray examination of the mixed crystals we used a Guinier-type focusing camera [19] and monochromatised Cu-K_α radiation from a bent quartz plate. To avoid shrinkage errors in the measurement of the Bragg angle θ, a 0·1 mm. scale was photographed on the film before processing.

Results and Discussion

Samples of 0—20 moles % of thorium tetrafluoride consisted, after heating, of two fluorite-type phases. As the diffraction photographs of these phases show no splitting of the cubic lines or any weak lines which could be attributed to a superlattice it seems that the oxygen and fluorine atoms in these mixed crystals are not ordered. The cell constant for these cubic phases was in the region from 5·586 ± 0·005 *kX*, the value for pure thoria, to 5·663 ± 0·005 *kX*. Therefore as thorium tetrafluoride is incorporated into the thoria lattice, the lattice expands.

Neither the solid solubility limit nor the mode of incorporation of the tetrafluoride in the thoria lattice could be determined experimentally as, even after long annealing, the mixed crystal phases were not homogeneous. However, by analogy with other systems, it would be expected that the extra anions ($2F^-$ replacing O^{2-}) needed for electric neutrality occupy interstitial positions in the lattice and that the cation lattice is intact. Similarly the limit of solid solubility of thorium tetrafluoride in thoria should be 25 moles %. The phase with a cell parameter of 5·663 is probably that at the limit of solid solubility.

Samples of 20—50 moles % of thorium tetrafluoride were again at least two-phase—thorium oxyfluoride and either one or two cubic phases with cell constants in the range given above. If only one cubic phase occurred with the oxyfluoride then the cell constant of this phase was 5·663. This supports the suggestion that the phase at the limit of solid solubility has a cell parameter of 5·663 *kX*.

Table 1. *Diffraction data for thorium oxyfluoride.*

Intensity	*hkl*	$\sin^2\theta$ (obs.)	$\sin^2\theta$ (calc.)	Intensity	*hkl*	$\sin^2\theta$ (obs.)	$\sin^2\theta$ (calc.)	Intensity	*hkl*	$\sin^2\theta$ (obs.)	$\sin^2\theta$ (calc.)
vw	200	0·0119	0·0120	vvw	501	0·0860	0·0859	vvw	512	0·1562	0·1559
w−	101	0·0142	0·0142	w+	402	0·0926	0·0928		021		0·1562
w	201	0·0232	0·0232	m	212	0·0930	0·0932	vvw	121	0·1594	0·1592
vvw	010	0·0369	0·0363	w+	411	0·0952	0·0953	vvw	313	0·1638	0·1644
vvw	301	0·0381	0·0381	w	103	0·1040	0·1043	vvw	221	0·1680	0·1682
s	002	0·0450	0·0450	w	600	0·1074	0·1076	vvw	503	0·1758	0·1760
m	011	0·0477	0·0475	vw	203	0·1128	0·1132	w+	004	0·1796	0·1800
	400		0·0478	vvw	502	0·1197	0·1197	vw	413	0·1852	0·1853
m+	102	0·0481	0·0480	vw	303	0·1279	0·1282	s	612	0·1886	0·1888
	210		0·0482	vw	412	0·1288	0·1290	m	022	0·1898	0·1900
vvw	111	0·0503	0·0504	vvw	113	0·1402	0·1405	w−	420	0·1925	0·1928
w−	202	0·0569	0·0569	s	610	0·1438	0·1438		122		0·1930
s	401	0·0590	0·0590	m	020	0·1450	0·1450	w	222	0·2025	0·2020
s	211	0·0593	0·0594	m−	403	0·1488	0·1491		801		0·2025
vvw	302	0·0717	0·0719	s−	213	0·1491	0·1495	m+	421	0·2039	0·2040
vvw	311	0·0739	0·0743	w	602	0·1523	0·1526		721	0·2276	0·2276
w	410	0·0840	0·0840					w	810		0·2275
	112		0·0842						404		0·2278
								w−	422	0·2380	0·2378

Samples of 50—100 moles % of tetrafluoride were two-phase, the oxyfluoride and tetrafluoride. No solid solubility of thoria in thorium tetrafluoride was observed.

Thorium Oxyfluoride.—The reflections with high intensity on the *X*-ray powder diffraction pattern of thorium oxyfluoride can be indexed in terms of the bimolecular

[19] D'Eye, U.K.A.E.A. Report A.E.R.E. C/R 1524 (1954); *Nature*, 1955, **175**, 623.

hexagonal cell suggested by Zachariasen. However there were many weak lines which could not be so accounted for and the reflections with indices *hk*0 and *hkl* are split. As the positions and intensities of the extra reflections and the line splitting are independent of the method of preparation of the sample these effects are not likely to be due to traces of impurity or to a solid solubility range. Indeed the *X*-ray photograph was successfully indexed on the basis of an orthorhombic unit cell with $a = 14{\cdot}07 \pm 0{\cdot}01$ *kX*, $b = 4{\cdot}041 \pm 0{\cdot}005$ *kX*, and $c = 7{\cdot}253 \pm 0{\cdot}005$ *kX*. The agreement between the calculated and observed values of $\sin^2\theta$ is good (Table 1). The observed indices of the reflections show that the *hk*0 planes are absent when $h = 2n + 1$. The volume of the unit cell is four times that of the bimolecular hexagonal cell and contains eight molecular units of $ThOF_2$. The pseudo-hexagonal indices which correspond to the orthorhombic indices of the reflections are given in Table 2.

The deviation from hexagonal symmetry can be accounted for by an ordering of the oxygen and fluorine atoms. The probable atomic arrangement in the ordered orthorhombic lattice can be derived by considering the atomic arrangement of the atoms in the larger of the two hexagonal cells. The atoms in the latter structure occupy the following special positions of space group D_{6h}^3—$P6_3/mcm$.; thorium on 6(*g*) and the anions on 2(*a*), 4(*c*), and 12(*k*). This structure can be considered to be made up of layers of cations and

TABLE 2. *Corresponding reflections.*

Orthorhombic	Pseudo-hexagonal	Orthorhombic	Pseudo-hexagonal
002	002	403	103
011, 400	100	213	
102, 210		004	004
401	101	612	112
211		022	
402	102	420	200
212		122	
610	110	222, 801	201
020		421	

anions with each cation surrounded by three anions and each anion by three cations. The anions in these layers occupy the positions 2(*a*) and 4(*c*) in the unit cell. Above and below each cation there is a further anion. These anions, which sit between the layers, occupy the position 12(*k*) and are not structurally equivalent to those in the layers. If the six oxygen atoms occupy the positions in the layers and the twelve fluorine atoms the positions between the layers, instead of both atoms being statistically distributed over all the eighteen anion sites, then the resultant lattice distortion will probably account for the deviation from hexagonal symmetry.

We could not prepare hexagonal thorium oxyfluoride which would have no ordering of the anions.

The author thanks Mr. E. A. Harper for help in the experimental work and Mrs. G. W. Stuart for taking the *X*-ray photographs.

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HARWELL, BERKSHIRE.

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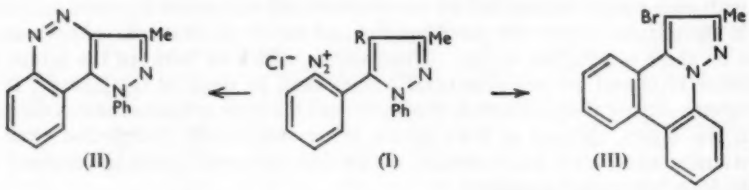
42. *The Reaction between Aroylacetones and Arylhydrazines.*

By I. L. Finar and Alma B. Simmonds.

o-, *m*-, and *p*-Nitrobenzoylacetones react with phenylhydrazine to form 3-methyl-5-*o*-, -*m*-, and -*p*-nitrophenyl-1-phenylpyrazoles only, whereas benzoylacetone and 2 : 4-dinitrophenylhydrazine give both 3- and 5-methyl-1-(2 : 4-dinitrophenyl)-5- and -3-phenylpyrazole. Evidence is given for the orientation of these pyrazoles and also of 3-*o*-aminophenyl-5-methyl-1-phenylpyrazole obtained from 4-chloroquinaldine and phenylhydrazine.

Misleading and inaccurate statements occur in various textbooks regarding the reaction of unsymmetrical β-diketones with monosubstituted hydrazines. Contrary to their expected behaviour, the simple β-diketones, R·CO·CH_2·COR′, do not generally form two isomeric pyrazoles. Only three such examples have so far been recorded: benzoylacetone and methylhydrazine,[1] 1-phenyl-4-*cyclo*propylbutane-1 : 3-dione and 2 : 4-dinitrophenylhydrazine,[2] and 3-benzoylacetyl-1 : 5-diphenylpyrazole and phenylhydrazine.[3] Further, when only one pyrazole has been isolated on reaction of an aroylacetone and an arylhydrazine, it has often been assumed to be the 1 : 5-diaryl-3-methylpyrazole,[4] by analogy with the reaction of benzoylacetone and phenylhydrazine.[5,6,7] So far, this assumption has been shown to be correct for the reaction between benzoylacetone and the three mononitrophenylhydrazines,[8] and for the three mononitrobenzoylacetones and phenylhydrazine.

The orientation of the 3-methyl-5-*m*- and -*p*-nitrophenyl-1-phenylpyrazoles was established by reduction to the amine, followed by diazotisation and treatment with hypophosphorous acid to give 3-methyl-1 : 5-diphenylpyrazole. In the same way, 3-methyl-5-*p*-nitrophenyl-1-phenylpyrazole-4-carboxylic acid can be reduced and deaminated to the known 3-methyl-1 : 5-diphenylpyrazole-4-carboxylic acid. On the other hand, 3-methyl-5-*o*-nitrophenyl-1-phenylpyrazole, when reduced, diazotised, and treated with hypophosphorous acid, gave 3′-methyl-1′-phenylpyrazolo(4′ : 5′-3 : 4)cinnoline (II),



(II) (I) (III)

instead of the expected methyldiphenylpyrazole. Cyclisation of the diazonium salt (I; R = H) is inhibited by concentrated acid and takes place spontaneously in dilute acid (cf. the Widman–Stoermer cinnoline synthesis [9]). Sodium hydroxide solution precipitated the cinnoline and also the ethanol-insoluble sodium diazoate. To prevent the formation of the cinnoline, the *o*-nitro-compound was converted into the 4-bromo-derivative. Reduction to the amine, followed by diazotisation and treatment of the

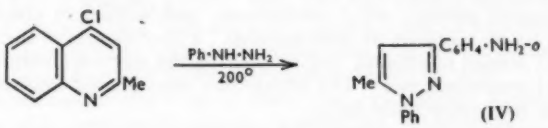
[1] Auwers and Stuhlmann, *Ber.*, 1926, **59**, 1054.
[2] Smith and Rogier, *J. Amer. Chem. Soc.*, 1951, **73**, 3834.
[3] Finar, *J.*, 1955, 1205.
[4] Bülow and Huss, *Ber.*, 1918, **51**, 399; Bull and Fuson, *J. Amer. Chem. Soc.*, 1933, **55**, 269; Schmid and Meyer, *Helv. Chim. Acta*, 1948, **31**, 748; Baker and Butt, *J.*, 1949, 2147; Schmid and Bolleter, *Helv. Chim. Acta*, 1950, **33**, 917.
[5] Knorr, *Ber.*, 1887, **20**, 1098.
[6] Drumm, *Proc. Roy. Irish Acad.*, 1931, **40**, *B*, 94.
[7] Knorr and Duden, *Ber.*, 1893, **26**, 111.
[8] Barry, Finar, and Simmonds, *J.*, 1956, 4974.
[9] Simpson, *J.*, 1943, 447.

diazonium salt (I; R = Br) with hypophosphorous acid, gave 4′-bromo-3′-methylpyrazolo(5′ : 1′-9 : 10)phenanthridine [8] (III).

In accordance with the directions of Koenigs and Freund,[10] *o*-nitrobenzoylacetone and phenylhydrazine were heated together in ethanol at 30—40°. Bright yellow crystals of the phenylhydrazone, m. p. 156°, were obtained. When, however, the diketone and phenylhydrazine were heated together in ethanol on a steam-bath, a colourless form of the phenylhydrazone, m. p. 136°, was obtained and 3-methyl-5-*o*-nitrophenyl-1-phenylpyrazole was isolated from the mother-liquor. A solution of the phenylhydrazone, m. p. 136°, in boiling ethanol, when quickly cooled, gave the phenylhydrazone, m. p. 156°. Both phenylhydrazones slowly formed 3-methyl-5-*o*-nitrophenyl-1-phenylpyrazole when heated in ethanol on a steam-bath.

When *o*-nitrobenzoylacetone or its phenylhydrazone was heated with an excess of phenylhydrazine, no trace of a bisphenylhydrazone was found. Gevekoht [11] claimed to have prepared the bisphenylhydrazone, m. p. 120°, but his analytical figures do not agree with the calculated values for it. Since our colourless phenylhydrazone melted at 120° when first isolated from the reaction mixture, Gevekoht's compound is probably an impure form of the monophenylhydrazone, m. p. 136°. To add to the confusion, Cohn has recorded Gevekoht's compound as 3-methyl-5-*o*-nitrophenyl-1-phenylpyrazole in his " Tabellarische Übersicht der Pyrazolderivate," Braunschweig, 1897. The formation of bisphenylhydrazones from β-diketones has not been observed, even when ring closure to a pyrazole is impossible as in the reaction between benzoylacetone and *N*-methyl-*N*-phenylhydrazine.[1]

When Koenigs and Freund [10] condensed *o*-nitrobenzoylacetone and phenylhydrazine in ethanol on a steam-bath, they obtained only the pyrazole which they named by analogy with the pyrazole formed from benzoylacetone and phenylhydrazine. Unfortunately, they followed Knorr's earlier ideas on the orientation of the isomeric methyldiphenylpyrazoles [5] and had overlooked the proofs of orientation given by Knorr and Duden,[7] and by Auwers and Mauss,[12] thus incorrectly naming their product 5-methyl-3-*o*-nitrophenyl-1-phenylpyrazole. Since their product gave on reduction a different amine from that formed by heating 4-chloroquinaldine with an excess of phenylhydrazine in a sealed tube at 200°, they named the product from the latter reaction as 5-*o*-aminophenyl-3-methyl-1-phenylpyrazole. We, however, have shown it to be 3-*o*-aminophenyl-5-methyl-1-phenylpyrazole (IV) by deamination to 5-methyl-1 : 3-diphenylpyrazole.

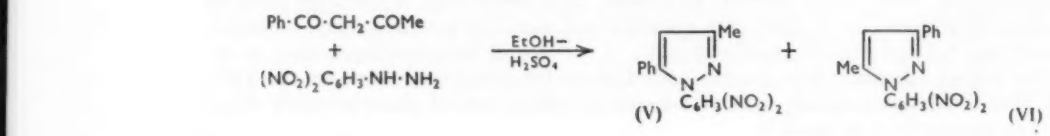


(IV)

We have now found another example of a simple β-diketone, benzoylacetone, which forms two pyrazoles with 2 : 4-dinitrophenylhydrazine. When Brady [13] carried out this reaction he obtained only one pyrazole, m. p. 151°, which he named 3(or 5)-methyl-1-(2 : 4-dinitrophenyl)-5(or 3)-phenylpyrazole. On the other hand Borsche and Reid [14] obtained from this reaction a pyrazole, m. p. 128—129°, and stated that it was 3-methyl-1-(2 : 4-dinitrophenyl)-5-phenylpyrazole. By this reaction we have isolated two isomeric pyrazoles, m. p. 154° and m. p. 137°, with the latter predominating. On several occasions, the product melted at 128°, but in every case it was separated into the two pyrazoles. Therefore, Borsche and Reid's product was undoubtedly a mixture. Henbest [15] prepared

[10] Koenigs and Freund, *Chem. Ber.*, 1947, **80**, 143.
[11] Gevekoht, *Annalen*, 1883, **221**, 323.
[12] Auwers and Mauss, *Ber.*, 1926, **59**, 611.
[13] Brady, *J.*, 1931, 756.
[14] Borsche and Reid, *Annalen*, 1943, **554**, 269.
[15] Henbest, *J.*, 1952, 4536.

(2 : 4-dinitrophenyl)-5-methyl-1-3-phenylpyrazole (VI), m. p. 154°, from phenyl propargyl ketone and 2 : 4-dinitrophenylhydrazine and gave evidence for its orientation. Brady's pyrazole is therefore (VI). The orientation of the isomeric pyrazole (V), m. p. 137°, has been independently established by reduction to the nitro-amine, followed by deamination to the known 3-methyl-1-*o*-nitrophenyl-5-phenylpyrazole.[8]



Experimental.

Additional Evidence for the Orientation of 3-*Methyl*-1 : 5-*diphenylpyrazole*.—The pyrazole was oxidised by boiling potassium permanganate in aqueous pyridine to 1 : 5-diphenylpyrazole-3-carboxylic acid which melted (alone or when mixed with an authentic specimen [3]) at 186°.

3-*Methyl*-5-o-*nitrophenyl*-1-*phenylpyrazole*.—*o*-Nitrobenzoylacetone (2·35 g., 0·0114 mole) and phenylhydrazine (1·3 g., 0·0114 mole), heated in ethanol at 35—40° for 10 min., gave bright yellow crystals (3·17 g., 93%) of the phenylhydrazone, m. p. 156° (Koenigs and Freund [10] give 163°) (Found: N, 14·3. Calc. for $C_{16}H_{15}O_3N_3$: N, 14·2%).

When, however the diketone (10 g., 0·05 mole) and phenylhydrazine (5·4 g., 0·05 mole) were separately dissolved in ethanol and then heated together on a steam-bath for 5 min., another form of the *phenylhydrazone* (6·4 g., 43%) was obtained as colourless flakes, m. p. 136° (Found: C, 64·4; H, 5·1; N, 14·0. $C_{16}H_{15}O_3N_3$ requires C, 64·6; H, 5·1; N, 14·2%), and the pyrazole [10,16] (7·5 g., 54%) of m. p. 95° was obtained from the mother-liquor. When the phenylhydrazone, m. p. 136°, was dissolved in boiling ethanol and quickly cooled, it was converted into the yellow form, m. p. 156°. Both phenylhydrazones slowly formed the pyrazole, m. p. 95°, when heated in ethanol on a steam-bath or recrystallised from chloroform, acetic acid, or benzene.

3-*Methyl*-5-m-*nitrophenyl*-1-*phenylpyrazole*.—*m*-Nitrobenzoylacetone (2·3 g., 0·011 mole) and phenylhydrazine (1·2 g., 0·011 mole), refluxed in ethanol for 3 hr., gave the *pyrazole* as pale yellow crystals (2·9 g., 93%), m. p. 102—103° (Found: C, 68·8; H, 4·8; N, 14·7. $C_{16}H_{13}O_2N_3$ requires C, 68·8; H, 4·8; N, 15·0%).

Ethyl p-*Nitrobenzoylacetoacetate*.—Bülow and Hailer [17] prepared this ester by reaction between *p*-nitrobenzoyl chloride, ethyl acetoacetate, and sodium in ethanol. We found it difficult to obtain a pure specimen by their method. A good sample of the ester was obtained by using methanol instead of ethanol, and by pouring the reaction mixture into ice-water to precipitate methyl *p*-nitrobenzoate. The filtrate was then poured into cooled glacial acetic acid and extracted with ether (yield 48%).

3-*Methyl*-5-p-*nitrophenyl*-1-*phenylpyrazole*-4-*carboxylic Acid*.—This acid was prepared from *p*-nitrobenzoylacetoacetic ester by Knorr and Jödicke's method [16]; it had m. p. 210° (Knorr and Jödicke give 202°).

3-*Methyl*-5-p-*nitrophenyl*-1-*phenylpyrazole*.—(*a*) The pyrazole was prepared by heating the 4-carboxylic acid for about 3 hr. at 240—250°. The pyrazole had the m. p. 111—112° (Knorr and Jödicke [18] obtained an oil). (*b*) *p*-Nitrobenzoylacetone (2 g., 0·01 mole) and phenylhydrazine (1·1 g., 0·01 mole), refluxed together in ethanol, gave the pyrazole (1·0 g., 36%) as yellow needles, m. p. 111° (Found: C, 68·8; H, 4·6; N, 14·9%).

1-(2 : 4-*Dinitrophenyl*)-3(*and* 5)-*methyl*-5(*and* 3)-*phenylpyrazoles*.—Benzoylacetone (20 g., 0·12 mole) in ethanol was added to a hot solution of 2 : 4-dinitrophenylhydrazine (16 g., 0·08 mole) in ethanol (350 c.c.) and 98% sulphuric acid (32 c.c.) and heated on a steam-bath for 10 min. Yellow plates of 1-(2 : 4-dinitrophenyl)-5-methyl-3-phenylpyrazole (VI) (2·1 g., 8%), m. p. 154° (from ethanol or acetic acid), were decanted from yellow needles of 1-(2 : 4-*dinitrophenyl*)-3-*methyl*-5-*phenylpyrazole* (V) (15·3 g., 67%), m. p. 137° (from ethanol or acetic acid) (Found: C, 59·2; H, 3·7; N, 16·8. $C_{16}H_{12}O_4N_4$ requires C, 59·3; H, 3·7; N, 17·3%).

[16] Knorr and Jödicke, *Ber.*, 1885, **18**, 2259.
[17] Bülow and Hailer, *Ber.*, 1902, **35**, 932.

4-Bromopyrazoles.—The pyrazole in glacial acetic acid was treated with an excess of bromine at room temperature. The precipitate was dissolved in chloroform, washed with sodium carbonate solution and water, and allowed to crystallise. 3-Methyl-5-*o*-nitrophenyl-1-phenylpyrazole (5 g.) gave the *4-bromo-derivative* (5·5 g., 86%), m. p. 141° (Found: Br, 22·0. $C_{16}H_{12}O_2N_3Br$ requires Br, 22·2%). 1-(2 : 4-Dinitrophenyl)-3-methyl-5-phenylpyrazole (V) (2·5 g.) gave the *4-bromo-derivative* (2·9 g., 93%), m. p. 176° (Found: Br, 19·9. $C_{16}H_{11}O_4N_4Br$ requires Br, 19·8%). 1-(2 : 4-Dinitrophenyl)-5-methyl-3-phenylpyrazole (VI) (1·15 g.) gave the *4-bromo-derivative* (1·3 g., 91%), m. p. 158° (Found: Br, 19·9%).

5-Aminophenyl-3-methyl-1-phenylpyrazoles.—The nitro-compound (1 mol.) in ethanol was heated on a steam-bath with stannous chloride (8 mol.) in concentrated hydrochloric acid for 1 hr. The solution was made alkaline with 30% ammonia solution, and the amine was extracted with ether and recrystallised from ethanol. The *m*-nitro-compound gave pale yellow crystals of the *amine*, m. p. 161·5° (Found: C, 77·0; H, 6·0; N, 16·3. $C_{16}H_{15}N_3$ requires C, 77·1; H, 6·0; N, 16·9%). The *p*-nitro-compound gave colourless crystals of the amine, m. p. 93°. The *o*-nitro-compound gave the amine,[10] m. p. 96° (yield 50%); a better product, m. p. 99°, was obtained when a solution of the *o*-nitro-compound (17·5 g.) in ethanol–hydrazine hydrate solution (60%; 10 c.c.) was heated in the presence of palladised charcoal (2 g.) on a steam-bath (yield 13 g., 83%).

5-o-Aminophenyl-4-bromo-3-methyl-1-phenylpyrazole.—The nitro-compound (10 g.), reduced with stannous chloride as above, gave colourless crystals of the *amine* (5·1 g., 54%), m. p. 135° (Found: C, 58·6; H, 4·4; N, 12·4; Br, 24·1. $C_{16}H_{14}N_3Br$ requires C, 58·5; H, 4·3; N, 12·8; Br, 24·4%).

5-p-Aminophenyl-3-methyl-1-phenylpyrazole-4-carboxylic Acid.—This compound, prepared by the method of Knorr and Jödicke,[16] had m. p. 261° (Knorr and Jödicke give m. p. 251°).

1-(4-Amino-2-nitrophenyl)-3-methyl-5-phenylpyrazole.—The dinitro-compound (V) (8 g.) in ethanol (500 c.c.) and 30% aqueous ammonia solution (15 c.c.) was saturated with hydrogen sulphide and heated on a steam-bath for 1 hr. The solution was evaporated to small bulk and the crystals obtained (5·3 g., 73%) were purified by dissolving them in concentrated hydrochloric acid and filtering. Addition of water gave bright yellow crystals of the *nitro-amine*, m. p. 182° (from ethanol) (Found: N, 18·7. $C_{16}H_{14}O_2N_4$ requires N, 19·0%).

1-(4-Amino-2-nitrophenyl)-5-methyl-3-phenylpyrazole.—The dinitro-compound (VI) (1·4 g.) in ethanol (60 c.c.) and 30% aqueous ammonia (3 c.c.) on reduction with hydrogen sulphide gave the *nitro-amine* (0·7 g., 54%), m. p. 170° (from ethanol or ligroin) (Found: C, 65·6; H, 4·5. $C_{16}H_{14}O_2N_4$ requires C, 65·3; H, 4·7%).

Diazotisation and Hypophosphorous Acid Treatment of the Aminophenylpyrazoles.—The amine (0·6 g.) was dissolved in concentrated hydrochloric acid (3 c.c.) and diazotised with sodium nitrite (0·3 g.) in water (0·5 c.c.). After ½ hr. the solution was poured into 30% hypophosphorous acid (7 c.c.). 5-*m*- and 5-*p*-Aminophenyl-3-methyl-1-phenylpyrazole both gave 3-methyl-1 : 5-diphenylpyrazole which was characterised as its bromo-derivative,[12, 18] m. p. 75°. 5-*p*-Aminophenyl-3-methyl-1-phenylpyrazole-4-carboxylic acid gave 3-methyl-1 : 5-diphenylpyrazole-4-carboxylic acid,[18] m. p. 205°. 3-*o*-Aminophenyl-5-methyl-1-phenylpyrazole (IV) gave 5-methyl-1 : 3-diphenylpyrazole, characterised as its picrate,[12] m. p. 108°. 5-*o*-Aminophenyl-3-methyl-1-phenylpyrazole gave *3′-methyl-1′-phenylpyrazolo*(4′ : 5′-3 : 4)*cinnoline* (II), m. p. 216°, which was also obtained when the diazonium salt solution was heated with ethanol and Gattermann copper powder or with boiling 50% sulphuric acid, or was made alkaline with sodium hydroxide solution (Found: C, 73·4; H, 4·7; N, 21·2. $C_{16}H_{12}N_4$ requires C, 73·8; H, 4·6; N, 21·5%). 5-*o*-Aminophenyl-4-bromo-3-methyl-1-phenylpyrazole gave 4′-bromo-3′-methylpyrazolo(5′ : 1′-9 : 10)phenanthridine [8] (III), m. p. 140° (Found: C, 61·7; H, 3·9; N, 8·7; Br, 25·3. Calc. for $C_{16}H_{11}N_2Br$: C, 61·7; H, 3·5; N, 9·0; Br, 25·7%). 1-(4-Amino-2-nitrophenyl)-3-methyl-5-phenylpyrazole gave red needles, m. p. 108°; it was successfully deaminated by adding the nitro-amine (1 g.) in glacial acetic acid (12 c.c.) to sodium nitrite (0·3 g.) in concentrated sulphuric acid (1·5 c.c.) at 5°. After ½ hr. the solution was heated with ethanol (20 c.c.) on a steam-bath for ½ hr. Dilution with water and extraction with ether gave pale yellow crystals which melted at 104° alone or when mixed with 3-methyl-1-*o*-nitrophenyl-5-phenylpyrazole.[8]

Knorr's Pyrazoline Reaction.—The aminophenylpyrazoles were reduced with sodium and ethanol, evaporated to dryness, and dissolved in concentrated sulphuric acid. On addition

[18] Knorr and Blank, *Ber.*, 1885, **18**, 316.

of sodium nitrite solution, 5-*o*-, -*m*-, and -*p*-aminophenyl-3-methyl-1-phenylpyrazoles, and 1-*o*-aminophenyl-3-methyl-5-phenylpyrazole [9] gave a red colour whereas 3-*o*-aminophenyl-5-methyl-1-phenylpyrazole gave a blue colour (cf. Knorr [10] and Auwers and Mauss [12]).

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LONDON, N.7.

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[10] KNORR, *Annalen*, 1887, **238**, 200; *Ber.*, 1893, **26**, 100.

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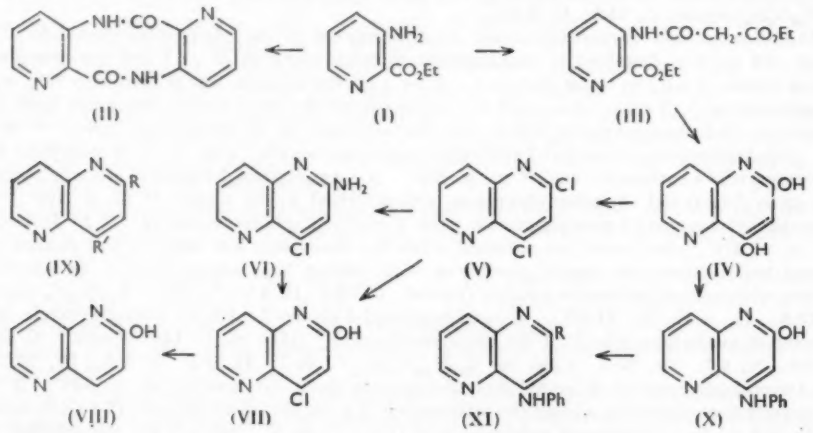
43. *Polyazanaphthalenes. Part V.* Some 2 : 4-Disubstituted 1 : 5-Naphthyridines.*

By V. OAKES and H. N. RYDON.

Several 2 : 4-disubstituted 1 : 5-naphthyridines have been synthesised by way of the 2 : 4-dihydroxy- and 2 : 4-dichloro-compounds. In agreement with the results of approximate quantum-mechanical calculations, the 2-chlorine atom in 2 : 4-dichloro-1 : 5-naphthyridine is more reactive than the 4-chlorine atom towards nucleophilic reagents, the compound resembling, in this respect, 2 : 4-dichloroquinoline rather than 2 : 4-dichloroquinazoline. In 2 : 4-dihydroxy-1 : 5-naphthyridine, however, the 4-hydroxyl group reacts with aniline in the presence of acid in preference to the 2-hydroxyl-group; an explanation of this apparent anomaly is proposed.

THE chemistry of 1 : 5-naphthyridine (1 : 5-diazanaphthalene) has been but little studied [1] and no disubstitution products containing reactive groupings in both the 2- and the 4-position have been described. As a preliminary to a projected synthesis of pteroic and folic acid analogues based on this ring system it was, therefore, essential first to investigate some simpler 2 : 4-disubstituted 1 : 5-naphthyridines; the present paper is concerned with this preliminary study.

The key intermediate required for our work was 2 : 4-dihydroxy-1 : 5-naphthyridine (IV). An attempt to prepare this by Claisen condensation of ethyl 3-aminopicolinate (I)



with ethyl acetate, followed by cyclisation, failed, intermolecular amidation, with production of 1 : 7-diazadianthranilide (II), taking precedence over the Claisen condensation; similar self-amidations resulting in the formation of dianthranilide derivatives

* Part IV, Oakes and Rydon, *J.*, 1956, 4433.

[1] For a review, see Allen, *Chem. Rev.*, 1950, **47**, 275.

have previously been observed with methyl 2-aminonicotinate [2] and methyl anthranilate.[3] 2 : 4-Dihydroxy-1 : 5-naphthyridine (IV) was finally prepared, in good yield, by an adaptation of a method [4] previously used for the synthesis of 2 : 4-dihydroxy-quinolines and -1 : 8-naphthyridines. Condensation of ethyl 3-aminopicolinate (I) with malonic ester gave the substituted malonamic ester (III), which readily underwent Dieckmann cyclisation; hydrolysis and decarboxylation then gave the required dihydroxy-compound (IV), which with phosphorus oxychloride readily yielded the dichloro-compound (V).

Application of the approximate quantum-mechanical treatment developed by Longuet-Higgins [5] and subsequently applied to heterocyclic chloro-compounds by Chapman [6] and ourselves [7] shows that 2 : 4-dichloro-1 : 5-naphthyridine should resemble 2 : 4-dichloro-quinoline, and differ from 2 : 4-dichloroquinazoline, in that the 2-chlorine atom should be the more reactive. The results of the calculations are tabulated, the symbolism being the same as that used in our earlier paper.[7]

2 : 4-Dichloro-derivative of	Nucleophilic substitution of	$\Delta U - \Delta U_0$	$\Delta U_{4Cl} - \Delta U_{2Cl}$
Quinazoline [7]	2-Cl	$0{\cdot}63\delta^N + 0{\cdot}08\delta^{Cl}$	$0{\cdot}10\delta^N + 0{\cdot}16\delta^{Cl} + \delta'$
	4-Cl	$0{\cdot}73\delta^N + 0{\cdot}24\delta^{Cl}$	
Quinoline	2-Cl	$0{\cdot}50\delta^N + 0{\cdot}08\delta^{Cl}$	$-0{\cdot}14\delta^N + 0{\cdot}16\delta^{Cl} + \delta'$
	4-Cl	$0{\cdot}36\delta^N + 0{\cdot}24\delta^{Cl}$	
1 : 5-Naphthyridine	2-Cl	$0{\cdot}58\delta^N + 0{\cdot}08\delta^{Cl}$	$-0{\cdot}15\delta^N + 0{\cdot}16\delta^{Cl} + \delta'$
	4-Cl	$0{\cdot}43\delta^N + 0{\cdot}24\delta^{Cl}$	

$\Delta U_{4Cl} - \Delta U_{2Cl}$ is a measure of the difference in activation energy, at 0° K, of the reactions of the 4- and the 2-chlorine atom with a given nucleophilic reagent; since δ is negative, and δ^N without doubt larger than δ^{Cl} and δ', it is clear that the 4-chlorine atom will be less reactive than the 2-chlorine atom in the 1 : 5-naphthyridine and quinoline derivatives, but more reactive in the quinazoline derivative. It is already known that the 2-chlorine atom is the more reactive of the two in 2 : 4-dichloroquinoline,[8,9,10] in agreement with the theoretical predictions, and our results now show that the same is true for 2 : 4-dichloro-1 : 5-naphthridine.*

The predicted preferential reactivity of the 2-chlorine atom in 2 : 4-dichloro-1 : 5-naphthyridine (V) towards nucleophilic reagents was exhibited in its reactions with ammonia, water, and hydrazine. With ethanolic ammonia at 170°, the sole product isolated was 2-amino-4-chloro-1 : 5-naphthyridine (VI), which was converted by nitrous acid into 4-chloro-2-hydroxy-1 : 5-naphthyridine (VII); the latter compound was also obtained directly from the dichloro-compound (V), by the action of aqueous hydrochloric acid, a reagent which similarly brings about preferential hydrolysis of the 2-chlorine atom in 2 : 4 : 7-trichloroquinoline.[12] The structures of the two monochloro-compounds (VI) and (VII) were established by conversion of the latter into 2-hydroxy-1 : 5-naphthyridine (VIII) by treatment with toluene-*p*-sulphonhydrazide, followed by alkali.[13] Hydrazine

* Dornow and von Loh [11] have recently shown that the 2-chlorine atom reacts preferentially with hydrazine in a number of 2 : 4-dichloro-1 : 8-naphthyridines; this finding, too, is in agreement with calculation ($\Delta U_{4Cl} - \Delta U_{2Cl} = -0{\cdot}18\delta^N + 0{\cdot}16\delta^{Cl} + \delta'$).

[2] Klisiecki and Sucharda, *Roczniki Chem.*, 1923, **3**, 251.
[3] Cooper and Partridge, *J.*, 1954, 3429.
[4] Koller, *Ber.*, 1927, **60**, 407, 1108; cf. Lutz, Ashburn, Freek, Jordan, Leake, Martin, Rowlett, and Wilson, *J. Amer. Chem. Soc.*, 1946, **68**, 1285.
[5] Longuet-Higgins, *J. Chem. Phys.*, 1950, **18**, 283; *Nature*, 1950, **166**, 139.
[6] Chapman, *Chem. Soc. Special Publ.* No. 3, 1955, p. 155; Chapman and Russell-Hill, *J.*, 1956, 1563.
[7] Oakes and Rydon, *J.*, 1956, 4433.
[8] Friedländer and Weinberg, *Ber.*, 1882, **15**, 2679.
[9] Buchmann and Hamilton, *J. Amer. Chem. Soc.*, 1942, **64**, 1357.
[10] Curd, Raison, and Rose, *J.*, 1947, 899.
[11] Dornow and von Loh, *Arch. Pharm.*, 1957, **290**, 136.
[12] Rowlett and Lutz, *J. Amer. Chem. Soc.*, 1946, **68**, 1288.
[13] Albert and Royer, *J.*, 1949, 1148.

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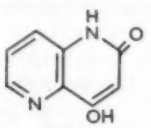
likewise replaces only one of the chlorine atoms of compound (V); the product is, beyond reasonable doubt, the 4-chloro-2-hydrazino-compound (IX; R = NH·NH_2, R′ = Cl). All attempts to replace both chlorine atoms by amino-groups were unsuccessful; treatment with ammonia in boiling phenol [14] gave only the diphenoxy-compound (IX; R = R′ = OPh), also obtained by heating with phenol alone, while ammoniacal copper sulphate [15] at 200° gave the 2-amino-4-hydroxy-compound (IX; R = NH_2, R′ = OH).

The differential reactivity of the two chlorine atoms in the dichloro-compound (V) is not exhibited in its reactions with aniline and benzylamine; here both chlorine atoms are replaced, with formation of the 2 : 4-dianilino- and the 2 : 4-dibenzylamino-compound (IX; R = R′ = NHPh and NH·CH_2Ph, respectively); even if only one mol. of aniline is used, in dioxan solution, the major product is the dianilino-compound. Attempts to prepare the diamino-compound (IX; R = R′ = NH_2) from the dibenzylamino-compound, by hydrogenolysis or by the action of sodium in liquid ammonia or of hydrogen bromide in acetic acid, were unsuccessful.

Curd, Raison, and Rose [10] obtained 4-arylamino-2-hydroxyquinolines by heating 2 : 4-dihydroxyquinoline with arylamines in the presence of their hydrochlorides. We have applied this reaction to 2 : 4-dihydroxy-1 : 5-naphthyridine (IV), obtaining a good yield of 4-anilino-2-hydroxy-1 : 5-naphthyridine (X); this structure is assigned on the basis of the insolubility of the product in alkali, a property it shares with 4-anilino-2-hydroxyquinoline, whereas 2-anilino-4-hydroxyquinoline is soluble in alkali.[10,16] In both 2 : 4-dihydroxy-1 : 5-naphthyridine and 2 : 4-dihydroxyquinoline, the preferential reactivity of the 4-hydroxyl group towards aniline is anomalous, since the 2-hydroxyl group would have been expected to be the more reactive towards nucleophilic reagents. However, spectroscopic evidence [17] suggests that 4-hydroxy-groups are more phenolic than 2-hydroxy-groups in both the quinoline and the pyridine series, and it seems likely that both 2 : 4-dihydroxy-compounds exist mainly as the 2-keto-tautomerides (XII) and (XIII); this formulation as vinylogues of carboxylic acids is supported by solubility of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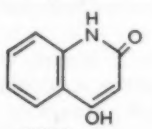
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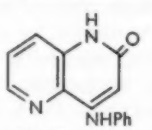
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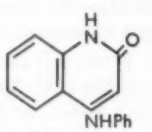
(XV)

these compounds in sodium hydrogen carbonate. The alkali-insolubility of 4-anilino-2-hydroxy-1 : 5-naphthyridine and -quinoline may similarly be due to the preponderance of the keto-forms (XIV) and (XV). The 4-anilino-2-hydroxy-compound, (X) or (XIV), could not be obtained by heating 4-chloro-2-hydroxy-1 : 5-naphthyridine (VII) with aniline; Buchmann and Hamilton [9] observed a similar lack of reactivity towards aniline of 4-chloro-2-hydroxyquinoline. Treatment of 4-anilino-2-hydroxy-1 : 5-naphthyridine (X) with phosphorus oxychloride gave the 4-anilino-2-chloro-compound (XI; R = Cl), which yielded 2-amino-4-anilino-1 : 5-naphthyridine (XI; R = NH_2) with ethanolic ammonia.

Experimental

1 : 7-*Diazadianthranilide* (II).—Ethyl 3-aminopicolinate [18] (3 g.), ethyl acetate (2·1 g.), and sodium ethoxide (1·8 g.) were heated together under reflux for 6 hr. The product was extracted with boiling water (2 × 50 ml.); the cooled extract deposited crystals, a further crop being

[14] Backeberg and Marais, *J.*, 1942, 381; Albert, Brown, and Duewell, *J.*, 1948, 1284; Brown, *J. Soc. Chem. Ind.*, 1950, **69**, 353.
[15] Hertog and Wibaut, *Rec. Trav. chim.*, 1936, **55**, 122.
[16] Dziewonski and Dymek, *Bull. int. Acad. polon. Sci. Lettres, Ser. A*, 1936, 413; *Chem. Zentr.*, 1937, I, 1153.
[17] Ewing and Steck, *J. Amer. Chem. Soc.*, 1946, **68**, 2181; Hertog and Buurman, *Rec. Trav. chim.*, 1956, **75**, 257.
[18] Oakes, Pascoe, and Rydon, *J.*, 1956, 1045.

obtained by adjusting the pH to 5·5. The *compound* (700 mg., 32%) crystallised from hot water or from formamide in needles, m. p. 382° (Found: C, 59·5; H, 3·4; N, 23·6. $C_{12}H_8O_2N_4$ requires C, 60·0; H, 3·3; N, 23·3%).

2 : 4-*Dihydroxy*-1 : 5-*naphthyridine* (IV).—Ethyl 3-aminopicolinate [18] (20 g.) was added in portions, under reflux, to malonic ester (150 ml.) at 100°, the alcohol formed being allowed to distil. When no more alcohol distilled, the excess of malonic ester was removed under reduced pressure and the cooled residue treated with anhydrous ether (100 ml.) and filtered. Addition of more ether (350 ml.) precipitated a pale yellow solid (1 g.), which was filtered off after 2 hr. and recrystallised from water; NN′-*di*-(2-*ethoxycarbonyl*-3-*pyridyl*)*malonamide* formed needles, m. p. 155° (Found: C, 57·3; H, 5·4; N, 13·9. $C_{19}H_{20}O_6N_4$ requires C, 57·0; H, 5·0; N, 14·0%). The ethereal filtrate was treated with ethanolic sodium ethoxide (from sodium, 3·5 g., and absolute ethanol, 100 ml.), and the mixture refluxed for 5 hr. Next day, the precipitated solid was filtered off, suspended in water (30 ml.), and refluxed with 40% sodium hydroxide solution (70 ml.) until effervescence ceased. Boiling water was added until an almost clear solution was obtained; this was filtered and acidified with acetic acid; the *dihydroxy-compound* (13·5 g., 69%) was thus obtained as a yellow solid, m. p. >360° (Found: C, 59·0; H, 3·7; N, 16·8. $C_8H_6O_2N_2$ requires C, 59·2; H, 3·7; N, 17·3%), soluble in 2N-sodium carbonate.

2 : 4-*Dichloro*-1 : 5-*naphthyridine* (V).—The dihydroxy-compound (5 g.) was refluxed for 6 hr. with phosphorus oxychloride (60 ml.). Excess of oxychloride was removed under reduced pressure and the residue treated with an excess of dilute aqueous ammonia. Filtration and sublimation at 160°/0·001 mm. afforded the *dichloro-compound* (5 g., 81%) as needles, m. p. 140° (Found: C, 48·4; H, 2·1; N, 13·8. $C_8H_4N_2Cl_2$ requires C, 48·2; H, 2·0; N, 14·1%).

2-*Amino*-4-*chloro*-1 : 5-*naphthyridine* (VI).—The dichloro-compound (400 mg.) was heated in a sealed tube with saturated ethanolic ammonia (10 ml.) for 20 hr. at 170°. Evaporation to dryness under reduced pressure, repeated washing with water, and drying at 100° afforded the *amino-chloro-compound* (170 mg., 47%), m. p. 184° (Found: N, 23·1. $C_8H_6N_3Cl$ requires N, 23·4%).

4-*Chloro*-2-*hydroxy*-1 : 5-*naphthyridine* (VII).—(*a*) A solution of the amino-chloro-compound (70 mg.) in water (3·5 ml.) containing sulphuric acid (0·7 ml.) was slowly treated, at 0°, with sodium nitrite (1 g.). After being heated at 100° for 30 min., the solution was made alkaline with sodium carbonate and evaporated to dryness under reduced pressure; sublimation at 170°/10^{-4} mm. afforded the chloro-hydroxy-compound, m. p. and mixed m. p. 263°.

(*b*) The dichloro-compound (500 mg.) was refluxed for 3 hr. with 5N-hydrochloric acid (6 ml.) and dioxan (4·5 ml.). The cooled mixture was poured into water (50 ml.) and made alkaline with sodium carbonate. After being kept overnight at 0°, the *chloro-hydroxy-compound* (300 mg., 66%) was collected and recrystallised from ethyl acetate, forming needles, m. p. 263° (Found: C, 53·2; H, 3·0; N, 16·2. $C_8H_5ON_2Cl$ requires C, 53·2; H, 2·8; N, 15·5%).

2-*Hydroxy*-1 : 5-*naphthyridine* (VIII).—The chloro-hydroxy-compound (100 mg.) was dissolved in a little chloroform and treated with a concentrated solution of toluene-*p*-sulphonhydrazide (300 mg.) in the same solvent. Dry hydrogen chloride was passed through the solution until precipitation was complete. After an hour the precipitate was collected and heated for 3 hr. with 10% sodium hydroxide solution (10 ml.). The cooled solution was saturated with carbon dioxide and evaporated to dryness under reduced pressure. Vacuum-sublimation afforded the hydroxy-compound, m. p. 258° (Found: N, 19·6. Calc. for $C_8H_6ON_2$: N, 19·2%) (lit.,[19, 20] m. p. 259°; lit.,[2, 20] m. p. of 4-hydroxy-1 : 5-naphthyridine, 340°).

4-*Chloro*-2-*hydrazino*-1 : 5-*naphthyridine* (IX; R = NH·NH_2, R′ = Cl).—The dichloro-compound (500 mg.) was refluxed for 16 hr. with hydrazine hydrate (1 ml.) in dioxan (20 ml.). Evaporation to dryness under reduced pressure and treatment of the residue with water afforded the *compound* (330 mg., 68%), which crystallised from water in needles, m. p. 162° (Found: C, 49·5; H, 3·6; N, 28·6. $C_8H_7N_4Cl$ requires C, 49·3; H, 3·6; N, 28·8%).

2 : 4-*Diphenoxy*-1 : 5-*naphthyridine* (IX; R = R′ = OPh).—The dichloro-compound (100 mg.) was refluxed with phenol (3 g.) for 6 hr. Treatment of the cooled product with 10% sodium hydroxide solution, followed by filtration, afforded the *diphenoxy-compound* (140 mg., 89%), which crystallised from light petroleum (b. p. 60—80°) in needles, m. p. 170° (Found: C, 76·7; H, 4·9; N, 9·0. $C_{20}H_{14}O_2N_2$ requires C, 76·5; H, 4·5; N, 8·9%). The same product was obtained when gaseous ammonia was passed through the refluxing mixture.

[19] Petrow and Sturgeon, *J.*, 1949, 1157.
[20] Hart, *J.*, 1954, 1879.

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2-Amino-4-hydroxy-1 : 5-naphthyridine (IX; R = NH_2, R′ = OH).—The dichloro-compound (450 mg.) was suspended in aqueous ammonia (*d* 0·880; 6 ml.) containing copper sulphate (100 mg.), and the mixture heated in a sealed tube at 200° for 90 hr. The cooled product was filtered and the dark green precipitate (370 mg.) extracted with hot water. Recrystallisation from hot water of the extracted material, which was soluble in both 2N-hydrochloric acid and 2N-sodium hydroxide but was precipitated from the latter with acetic acid, afforded the *amino-hydroxy-compound* (300 mg., 83%) as pale yellow prisms, m. p. 320° (Found: C, 59·6; H, 4·6; N, 26·3. $C_8H_7ON_3$ requires C, 59·6; H, 4·3; N, 26·1%).

2 : 4-Dianilino-1 : 5-naphthyridine (IX; R = R′ = NHPh).—(*a*) The dichloro-compound (500 mg.) was heated at 180° with aniline (3 ml.) for 5 hr. The cooled product was treated with benzene, and the precipitated solid washed with benzene and then with water; recrystallisation from water afforded the *monohydrochloride* (750 mg., 86%), m. p. 253° (Found: C, 68·8; H, 5·1; N, 16·5. $C_{20}H_{17}N_4Cl$ requires C, 68·9; H, 4·9; N, 16·1%). Treatment of a hot aqueous solution with excess sodium hydroxide liberated the *base*, m. p. 153° (Found: C, 76·6; H, 5·2; N, 17·9. $C_{20}H_{16}N_4$ requires C, 77·0; H, 5·1; N, 17·9%).

(*b*) The dichloro-compound (500 mg.) and aniline (233 mg., 0·5 mol.) were refluxed together in dioxan (25 ml.) for 48 hr. A yellow hydrochloride (250 mg., 57%) separated from the cooled mixture; basification of an aqueous solution afforded the dianilino-compound, m. p. and mixed m. p. 152°.

2 : 4-Dibenzylamino-1 : 5-naphthyridine (IX; R = R′ = CH_2Ph).—The dichloro-compound (500 mg.) was heated at 190° with benzylamine (5 ml.) for 4 hr. The product was evaporated to dryness under reduced pressure and the residue treated with benzene (10 ml.). Benzylamine hydrochloride was filtered off; addition of light petroleum (b. p. 60—80°) to the filtrate afforded the *dibenzylamino-compound* (750 mg., 88%), m. p. 147° (Found: C, 77·6; H, 6·2. $C_{32}H_{30}N_4$ requires C, 77·7; H, 5·9%). Treatment with hydrogen bromide in acetic acid, followed by precipitation with ether, afforded the *monohydrobromide*, which crystallised from water in prisms, m. p. 216° (Found: C, 62·5; H, 4·8; N, 13·8; Br, 18·6. $C_{22}H_{21}N_4Br$ requires C, 62·8; N, 5·0; N, 13·3; Br, 19·0%).

4-Anilino-2-hydroxy-1 : 5-naphthyridine (X).—2 : 4-Dihydroxy-1 : 5-naphthyridine (1·6 g.) was refluxed for 12 hr. with aniline (4·6 g.) and aniline hydrochloride (1·3 g.). The cooled product was treated with a little ethanol, and the solid washed with ethanol until colourless and then with water until free from chloride ions. The residual *base* (2·05 g., 88%) crystallised from ethanol in leaflets, m. p. 251° (Found: N, 17·8. $C_{14}H_{11}ON_3$ requires N, 17·7%); it is insoluble in 10% sodium hydroxide solution.

4-Anilino-2-chloro-1 : 5-naphthyridine (XI; R = Cl).—The anilino-hydroxy-compound (1 g.) was refluxed for 2 hr. with phosphorus oxychloride (30 ml.). Excess of oxychloride was removed under reduced pressure and the oily residue dissolved in ethanol (5 ml.); addition of aqueous ammonia precipitated the *base* (920 mg., 85%) which, purified by sublimation at 150°/0·01 mm., had m. p. 146° (Found: C, 65·8; H, 4·5; N, 16·7. $C_{14}H_{10}N_3Cl$ requires C, 65·8; H, 3·9; N, 16·4%).

2-Amino-4-anilino-1 : 5-naphthyridine (XI; R = NH_2).—The anilino-chloro-compound (500 mg.) was heated in a sealed tube at 170° with saturated ethanolic ammonia (10 ml.) for 80 hr. The cooled product was evaporated to dryness under reduced pressure, the residue treated with water and filtered, and the filtrate basified with sodium hydroxide. The precipitated *base* (280 mg., 61%) crystallised from benzene–light petroleum (b. p. 60—80°) in long needles, m. p. 152° (Found: C, 70·8; H, 5·1; N, 23·7. $C_{14}H_{12}N_4$ requires C, 71·2; H, 5·1; N, 23·7%).

W are greatly indebted to the Anchor Chemical Co. Ltd. for a maintenance allowance (to V. O.). The microanalyses were carried out under the supervision of Mr. V. Manohin.

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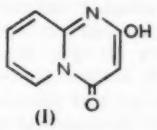
44. *Polyazanaphthalenes. Part VI.* Some Derivatives of 4 : 10-Dihydro-4-oxo-1 : 10-diazanaphthalene.*

By V. Oakes and H. N. Rydon.

Some derivatives of 4 : 10-dihydro-4-oxo-1 : 10-diazanaphthalene, with substituents in the 2- and the 3-position, have been prepared from the 2-hydroxy-4-oxo-compound (malonyl-α-aminopyridine).

Snyder and Robison [1] obtained a monochloro-compound by treatment of 4 : 10-dihydro-2-hydroxy-4-oxo-1 : 10-diazanaphthalene [2] (I) (or a tautomer) with phosphorus oxychloride; they assigned the structure (II; R = Cl) to this product on both spectroscopic and chemical grounds. We have improved the yield of this product and shown that, as expected, it reacts readily with nucleophilic reagents, *e.g.*, hydrazine, ammonia, and sodium methoxide, affording the hydrazino-, amino-, and methoxy-compounds (II; R = $NH{\cdot}NH_2$, NH_2, and OMe), respectively. Some confirmation of the structure (II; R = Cl) for the monochloro-compound was obtained by oxidation of the hydrazino-compound with copper sulphate [3] which gave a product, albeit in very poor yield, with properties corresponding to those of the 4-oxo-compound [4] (II; R = H) rather than to those of the 2-oxo-compound [5] (III).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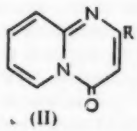
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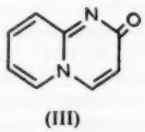
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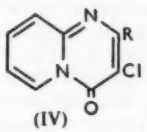
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By treatment of the starting material (I) with a mixture of phosphorus oxychloride and pentachloride, Snyder and Robison [1] obtained a second monochloro-compound (IV; R = OH) and a dichloro-compound (IV; R = Cl). We have improved the preparation of the dichloro-compound and shown that, again in agreement with expectation, only one of the two chlorine atoms is reactive towards nucleophilic reagents, treatment with ammonia, aniline, and phenol yielding the 2-amino-, 2-anilino-, and 2-phenoxy-compounds (IV; R = NH_2, NHPh, and OPh) respectively. Deamination of the amino-compound with nitrous acid afforded a monochloro-compound (IV; R = OH), identical with Snyder and Robison's second monochloro-compound.

In an attempt to obtain 4-arylamino-derivatives, the compound (I) was heated with aniline and with *p*-chloroaniline, in the presence of their hydrochlorides; [6] under the reaction conditions, however, the bicyclic structure was broken down, the only isolated products being malonanilide and the *p*-chloromalonanilide, respectively.

Experimental

2-Chloro-4 : 10-dihydro-4-oxo-1 : 10-diazanaphthalene (II; R = Cl).—4 : 10-Dihydro-2-hydroxy-4-oxo-1 : 10-diazanaphthalene (malonyl-α-aminopyridine) [2] (4 g.) was refluxed with phosphorus oxychloride (60 ml.) for 5 hr. Excess of oxychloride was removed under reduced pressure and the residue treated with 10% sodium hydrogen carbonate solution. The solid product was dried and sublimed at 160°/10^{-3} mm., affording the monochloro-compound (3 g., 67%), m. p. 159° (Found: C, 53·7; H, 2·9; N, 15·6. Calc. for $C_8H_5ON_2Cl$: C, 53·2; H, 2·8; N, 15·5%) (lit.,[1] m. p. 155—156°).

* Part V, preceding paper.

[1] Snyder and Robison, *J. Amer. Chem. Soc.*, 1952, **74**, 4910.
[2] Tschitschibabin, *Ber.*, 1924, **57**, 1168.
[3] Cf. Baumgarten and Su, *J. Amer. Chem. Soc.*, 1952, **74**, 3828.
[4] Adams and Pachter, *ibid.*, p. 5491.
[5] *Idem, ibid.*, p. 4906.
[6] Curd, Raison, and Rose, *J.*, 1947, 899.

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2-*Hydrazino*-4 : 10-*dihydro*-4-*oxo*-1 : 10-*diazanaphthalene* (II; R = NH·NH_2).—The monochloro-compound (2 g.) was heated under reflux on a water-bath for 2 hr. with hydrazine hydrate (4 g.) in dioxan (50 ml.). After cooling, the solid was collected and washed with water; recrystallisation from water gave the *hydrazino-compound* (1·75 g., 90%) as needles, m. p. 245° (Found: C, 54·6; H, 4·2. $C_8H_8ON_4$ requires C, 54·6; H, 4·6%).

4 : 10-*Dihydro*-4-*oxo*-1 : 10-*diazanaphthalene* (II; R = H).—The hydrazino-compound (1 g.), in water (40 ml.) containing acetic acid (10 ml.), was heated to boiling and treated slowly with 15% copper sulphate solution. After 30 minutes' refluxing, the solution was evaporated under reduced pressure and the residue sublimed at 140°/10^{-3} mm., affording the 4-oxo-compound (50 mg., 6%), m. p. 129° (lit.,[4] m. p. 127°, lit.[5] for the 2-oxo-compound, 248°) (Found: C, 65·4; H, 4·3; N, 18·9. Calc. for $C_8H_6ON_2$: C, 65·8; H, 4·1; N, 19·2%).

2-*Amino*-4 : 10-*dihydro*-4-*oxo*-1 : 10-*diazanaphthalene* (II; R = NH_2).—The monochloro-compound (1 g.) was heated at 170° for 16 hr. with saturated ethanolic ammonia (10 ml.). The cooled mixture was filtered and the solid product washed with water until chloride-free. Sublimation at 160°/10^{-4} mm. gave the *amino-compound* (350 mg., 39%), m. p. 257° (Found: C, 60·1; H, 4·3; N, 26·0. $C_8H_7ON_3$ requires C, 59·7; H, 4·4; N, 26·1%); the *picrate* crystallised from ethanol in needles, m. p. 222° (Found: C, 42·3; H, 2·3; N, 21·7. $C_{14}H_{10}O_8N_6$ requires C, 43·1; H, 2·6; N, 21·6%).

4 : 10-*Dihydro*-2-*methoxy*-4-*oxo*-1 : 10-*diazanaphthalene* (II; R = OMe).—The monochloro-compound (540 mg.) was refluxed for 4 hr. with sodium methoxide (from sodium, 80 mg., and methanol, 25 ml.). The product was evaporated to dryness under reduced pressure and the residue extracted with benzene. Evaporation of the extract afforded the *methoxy-compound* (475 mg., 90%), which crystallised from light petroleum (b. p. 60—80°) in needles, m. p. 146° (Found: C, 61·2; H, 4·5; N, 15·4. $C_9H_8O_2N_2$ requires C, 61·4; H, 4·6; N, 15·9%).

2 : 3-*Dichloro*-4 : 10-*dihydro*-4-*oxo*-1 : 10-*diazanaphthalene* (IV; R = Cl).—The compound (I) (10 g.) was refluxed for 5 hr. with phosphorus pentachloride (30 g.) and phosphorus oxychloride (120 g.). Excess of oxychloride was removed under reduced pressure and the residue cooled and treated with 10% sodium hydrogen carbonate solution. The yellow solid was filtered off and sublimed at 170°/10^{-4} mm.; the dichloro-compound (11·8 g., 89%) crystallised from ethanol in yellow needles, m. p. 230° (lit.,[1] m. p. 226—226·5°) (Found: C, 45·0; H, 1·7; N, 13·5; Cl, 32·6. Calc. for $C_8H_4ON_2Cl_2$: C, 44·7; H, 1·9; N, 13·0; Cl, 33·0%).

2-*Amino*-3-*chloro*-4 : 10-*dihydro*-4-*oxo*-1 : 10-*diazanaphthalene* (IV; R = NH_2).—The dichloro-compound (2 g.) was heated at 170° for 16 hr. with saturated ethanolic ammonia (10 ml.). After cooling, the crystals were collected, washed with water until chloride-free, and dried at 100°; the *amino-chloro-compound* (1·7 g., 93%) crystallised from ethanol in needles, m. p. 254° (Found: C, 48·9; H, 3·2; N, 21·6; Cl, 18·1. $C_8H_6ON_3Cl$ requires C, 49·15; H, 3·1; N, 21·5; Cl, 18·1%).

When ammonia was passed for 6 hr. through a boiling solution of the dichloro-compound (1 g.) in phenol (10 g.), the only isolated products were the amino-chloro-compound (390 mg., 43%), m. p. 254°, and the phenoxy-compound (see below) (290 mg., 23%), m. p. 148°.

3-*Chloro*-4 : 10-*dihydro*-2-*hydroxy*-4-*oxo*-1 : 10-*diazanaphthalene* (IV; R = OH).—The amino-chloro-compound (1 g.), in water (20 ml.) containing sulphuric acid (7 g.), was treated dropwise, at 0°, with sodium nitrite (6 g.) in water (15 ml.). After 1 hr., the monochloro-compound separated as a cream-coloured solid (930 mg., 93%) which, sublimed at 170°/10^{-4} mm., had m. p. 310° (lit.,[1] decomp. 290°) (Found: C, 48·7; H, 2·4. Calc. for $C_8H_5O_2N_2Cl$: C, 48·9; H, 2·55%).

2-*Anilino*-3-*chloro*-4 : 10-*dihydro*-1 : 10-*diazanaphthalene* (IV; R = NHPh).— The dichloro-compound (500 mg.) was heated at 100° for 5 hr. with aniline (500 mg.) in 50% acetic acid (10 ml.). On cooling, the *anilino-compound* (450 mg., 71%) separated in needles and was recrystallised from ethanol or from aqueous dioxan, forming leaflets, m. p. 195° (Found: C, 62·3; H, 3·6; N, 15·3; Cl, 13·5. $C_{14}H_{10}ON_3Cl$ requires C, 61·9; H, 3·7; N, 15·5; Cl. 13·05%).

3-*Chloro*-4 : 10-*dihydro*-4-*oxo*-2-*phenoxy*-1 : 10-*diazanaphthalene* (IV; R = OPh).—The dichloro-compound (200 mg.) was refluxed with phenol (5 g.) for 4 hr. The product was cooled to about 80° and added to excess of 10% sodium hydroxide solution. After cooling, the precipitated *phenoxy-compound* (225 mg., 89%) was collected, washed with water, and recrystallised from ethanol, forming needles, m. p. 148° (Found: C, 61·6; H, 3·2; N, 10·7. $C_{14}H_9O_2N_2Cl$ requires C, 61·7; H, 3·3; N, 10·3%).

Action of Arylamines on Malonyl-α-aminopyridine (I).—(*a*) This compound [2] (1·6 g.) was

refluxed for 12 hr. with aniline (4·6 g.) and aniline hydrochloride (1·3 g.). The cooled product was triturated with ethanol (10 ml.) and washed with ethanol and water until chloride-free; recrystallisation of the product from ethanol afforded malonanilide in needles, m. p. and mixed m. p. 227°.

(*b*) Malonylaminopyridine (1·6 g.) was heated at 190° for 12 hr. with *p*-chloroaniline (6·4 g.) and its hydrochloride (1·6 g.). Working up as before gave *p*-chloromalonanilide (1·75 g., 55%), needles (from ethanol), m. p. 259 (lit.,[7] m. p. 259°) (Found: C, 56·1; H, 3·9; N, 9·1; Cl, 21·8. Calc. for $C_{15}H_{12}O_2N_2Cl_2$: C, 55·8; H, 3·7; N, 8·7; Cl, 22·0%).

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MANCHESTER, 1.

[*Received, August 9th*, 1957.]

[7] Pauw, *Rec. Trav. chim.*, 1936, **55**, 215.

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45. *The Photolysis of Pyridoxal Phosphate.*

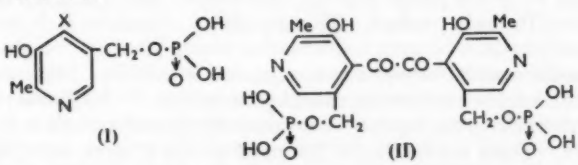
By A. L. MORRISON and R. F. LONG.

Pyridoxal phosphate, the co-factor of many enzymes involved in amino-acid metabolism, has been found to undergo a rapid, benzoin type, self-condensation in oxygen-free solution when exposed to light. The main product isolated was shown to be 5 : 5′-bis(dihydroxyphosphinyloxymethyl)-3 : 3′-dihydroxy-2 : 2′-dimethyl-4 : 4′-pyridil, presumably formed from the corresponding pyridoin during working up in the presence of air.

AQUEOUS solutions of pure crystalline pyridoxal phosphate monohydrate[1] (I; X = CHO) were found to decompose rapidly when exposed to sunlight or irradiated with ultraviolet light. Dilute solutions (*ca.* 0·5%) in air-free water under nitrogen, exposed to strong summer sunlight in 100 ml. Pyrex flasks, were completely photolysed in one hour. Little difference in the rate of reaction was observed between pH 2·0 and pH 8·0.

The photolysis was followed by measuring the ultraviolet absorption spectra of the solutions at pH 7·0 in phosphate buffer, the characteristic maximum of pyridoxal phosphate at 387 mμ being replaced by one of approximately equal intensity at 288 mμ. In acid or in alkaline solution the difference between the spectra of pyridoxal phosphate and its photolysed solution was much less marked.

By fractionation on a carboxylic acid ion-exchange resin, the principal product of the reaction was isolated in 75—88% yield, as colourless, high-melting crystals with an elementary analysis approximating to that of pyridoxal phosphate. It was almost insoluble in water and most organic solvents but dissolved readily in aqueous alkali to intensely yellow solutions.



(I) (II)

The presence of one carbonyl group per atom of phosphorus in the molecule was established by preparing an oxime with a N : P ratio of 2 : 1. Whereas pyridoxal phosphate reacts rapidly with hydroxylamine at room temperature, the oxime of the photolysis product was formed only on several hours' boiling. The reactive 4-formyl group of pyridoxal phosphate had therefore been altered.

[1] Peterson and Sober, *J. Amer. Chem. Soc.*, 1954, **76**, 169; Long, B.P. 749,800.

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Oxidation of pyridoxal phosphate with alkaline hydrogen peroxide gives 3 : 4-dihydroxy-2-methyl-5-pyridylmethyl dihydrogen phosphate [2] (I; X = OH). Oxidation of the photolysis product by this method gave a tribasic acid, identical with the compound made by oxidising pyridoxamine 5-(dihydrogen phosphate) (I; X = $CH_2 \cdot NH_2$) with excess of manganese dioxide at pH 2·0. This acid was shown to be 4-carboxy-3-hydroxy-2-methyl-5-pyridylmethyl dihydrogen phosphate (4-pyridoxic acid phosphate) (I; X = CO_2H), hydrolysis with concentrated hydrochloric acid giving the known lactone [3] of 4-carboxy-3-hydroxy-5-hydroxymethyl-2-methylpyridine. Since *o*-phenolic aldehydes on oxidation with alkaline hydrogen peroxide invariably give *o*-dihydroxy-compounds,[4] oxidation of the photolysed pyridoxal phosphate to a pyridine-4-carboxylic acid suggested that, while a carbonyl group was still in the 4-position in this compound, it was no longer part of an aldehyde. Oxidation with hydrogen peroxide in alkaline solution, followed by electrophoresis on filter paper, can be used to detect photolysis of pyridoxal phosphate since the phosphate of the carboxylic acid is separated readily from that of the dihydric phenol.

The photolysis product was reduced with sodium borohydride to a glycol, isolated in two fractions each associated with borate, and apparently differing only in the ease with which this was removed. Both forms gave pyridoxal phosphate on oxidation with periodate and were therefore presumably stereoisomers of 5 : 5′-bis(dihydroxyphosphinyloxymethyl)-3 : 3′-dihydroxy-2 : 2′-dimethyl-4 : 4′-hydropyridoin which has two asymmetric carbon atoms. In the oxidation, 1·2 moles of periodate per mole of glycol were used. Subsequently it was found that pyridoxal phosphate consumes 0·15 mole of periodate per mole under identical conditions. Comparison of the reaction mixtures by electrophoresis on filter paper showed them to have the same qualitative composition.

From these experiments it was concluded that the compound being investigated was 5 : 5′-bis(dihydroxyphosphinyloxymethyl)-3 : 3′-dihydroxy-2 : 2′-dimethyl-4 : 4′-pyridil (II). This was confirmed by oxidising the compound with sodium periodate to 4-pyridoxic acid 5-(dihydrogen phosphate) as the only product, the periodate uptake being 0·5 mole per atom of nitrogen. This reaction was extremely fast, in contrast to the oxidation of benzil which requires some days for completion.[5] Under the influence of light and in the absence of air pyridoxal phosphate therefore undergoes a benzoin condensation. The substitution in all four α-positions of the pyridoin initially formed would be expected to stabilise the ene-diol structure,[6] and the oxidation of ene-diol forms of α-pyridoins by atmospheric oxygen has been described by Eistert and Munder.[7] The isolation of a pyridil rather than a pyridoin is therefore not surprising.

The lack of colour in the solid pyridil is in keeping with previous observations that benzils with *o*-hydroxy-substituents can exist in stable, colourless modifications.[8]

When pyridoxal phosphate is decomposed by light in the presence of air, the pyridil (II) is always accompanied by some 4-pyridoxic acid 5-(dihydrogen phosphate). If a vigorous stream of oxygen is passed through the solution undergoing photolysis, the carboxylic acid becomes the only product. Thus pyridoxal phosphate is decomposed by light similarly to benzaldehyde, a benzoin condensation taking place in the absence of oxygen whereas a carboxylic acid is formed when oxygen is available. The mechanism of the photolysis of benzaldehyde has been discussed by Bäckström.[9] Pyridoxal phosphate differs from benzaldehyde in the great rapidity of its anærobic photolysis and in giving a dimer as the main product. From benzaldehyde the main products have been reported to be a

[2] Heyl, Luz, Harris, and Folkers, *J. Amer. Chem. Soc.*, 1951, **73**, 3434.
[3] Huff and Perlzweig, *J. Biol. Chem.*, 1944, **155**, 345.
[4] Dakin, *Amer. Chem. J.*, 1909, **42**, 486.
[5] Clutterbuck and Reuter, *J.*, 1935, 1467.
[6] Ide and Buek, "Organic Reactions," Vol. IV, p. 271.
[7] Eistert and Munder, *Chem. Ber.*, 1955, **88**, 215.
[8] Marsh and Stephen, *J.*, 1925, **127**, 1633.
[9] Bäckström, *Z. phys. Chem.*, 1934, **25**, 99.

tetramer and a trimer,[10] only small amounts of benzoin being obtained.[9] Benzoin has also been identified by Terenin[11] as a product of photochemical decomposition of benzaldehyde. Steric hindrance would probably suffice to prevent further condensation of the pyridoin derived from pyridoxal phosphate. Ultraviolet irradiation of acetaldehyde in aqueous solution has been reported[12] to give quantitative yields of acetoin.

Since pyridoxal phosphate is readily photolysed, it is important to protect this substance from strong light, particularly when in solution. Photolysis can be readily detected by the change in ultraviolet absorption spectrum of the substance. The pyridil is incapable of reactivating dissociated cysteinesulphinic acid decarboxylase, but does not compete with pyridoxal phosphate for this enzyme.[13]

Experimental

Photolysis of Pyridoxal Phosphate.—Pyridoxal phosphate monohydrate (0·53 g., 0·002 mole) was dissolved in 100 ml. of air-free water containing hydrochloric acid or sodium hydroxide to give solutions of pH 2, 4, 6, and 8 severally, which were exposed to bright summer sunlight for 1 hr. in stoppered Pyrex flasks, and their ultraviolet absorption spectra were measured at pH 7·0. The values tabulated did not change significantly after exposure to sunlight for a further hour.

	$E^{1\%}_{1\,cm.}$				
Wavelength	Pyridoxal		Photolysed solution		
(mμ)	phosphate . pH	2	4	6	8
288	30	199	195	192	209
329	99	82	86	69	58
387	202	50	44	52	82

A solution of pyridoxal phosphate monohydrate (5·3 g., 0·02 mole) in 250 ml. of air-free water containing 0·03 equivalent of sodium hydroxide was exposed to sunlight as in the previous experiment for 3 hr. It was then concentrated under reduced pressure to 50 ml. and run on to a column of Amberlite XE 97 cationic exchange resin (4 × 60 cm.). Water was passed through the column, the eluate being collected in 10 ml. fractions and the course of elution followed by making light-absorption measurements at 290 and 387 mμ at pH 7·0. Three products, isolated by evaporating appropriate fractions, corresponded to three spots observed when the photolysed solution was subjected to electrophoresis on filter paper. Two of these substances were present in amounts less than 20 mg. and were not examined further. The third substance which crystallised during evaporation was *5 : 5′-bis(dihydroxyphosphinyloxymethyl)-3 : 3′-dihydroxy-2 : 2′-dimethyl-4 : 4′-pyridil monohydrate* (II) (4·6 g.), m. p. 235—240° (Found: C, 36·0; H, 4·25; N, 5·4; P, 11·7. $C_{16}H_{18}O_{12}N_2P_2,H_2O$ requires C, 36·4; H, 3·9; N, 5·5; P, 12·1%).

Pyridoxal phosphate had the following absorption spectra: in phosphate buffer (pH 7·0) $\lambda_{min.}$ 289—290 (ε 770), $\lambda_{max.}$ 329—330 (ε 2610), $\lambda_{min.}$ 338—340 (ε 2510), $\lambda_{max.}$ 387—388 mμ (ε 5320); in 0·1N-NaOH $\lambda_{min.}$ 288—290 (ε 700), $\lambda_{max.}$ 306—307 (ε 900), $\lambda_{min.}$ 318 (ε 820), $\lambda_{max.}$ 388 mμ (ε 6500); in 0·1N-HCl $\lambda_{min.}$ 247—248 (ε 800), $\lambda_{max.}$ 294—295 (ε 7350), $\lambda_{min.}$ 318—319 (ε 1120), $\lambda_{max.}$ 335 mμ (ε 1380).

The absorption spectra of the pyridil were: in phosphate buffer (pH 7·0) $\lambda_{max.}$ 288—289 (ε 5300), $\lambda_{min.}$ 320 (ε 600), $\lambda_{max.}$ 334—338 (ε 650), $\lambda_{min.}$ 356—360 (ε 620), $\lambda_{max.}$ 388—394 mμ (ε 700); in 0·1N-NaOH $\lambda_{min.}$ 317 (ε 1350), $\lambda_{max.}$ 390—394 mμ (ε 5300); in 0·1N-HCl $\lambda_{min.}$ 263 (ε 1270), $\lambda_{max.}$ 295 mμ (ε 8000).

Pyridil Oxime.—The pyridil (II) (500 mg.) in 2N-aqueous sodium carbonate (20 ml.) was boiled under nitrogen for 3 hr. with hydroxylamine hydrochloride (1·0 g.). The solution was brought to pH 3 with 2N-hydrochloric acid, and the precipitate collected and washed with boiling water (100 ml.), to give the *dioxime dihydrate* (350 mg.), decomp. 212—214° (Found: C, 35·2; H, 4·7; N, 10·2; P, 11·15. $C_{16}H_{20}O_{12}N_4P_2,2H_2O$ requires C, 35·5; H, 4·1; N, 10·4; P, 11·5%), $\lambda_{max.}$ 330 (ε 4620), $\lambda_{min.}$ 274 mμ (ε 2170) at pH 7·0.

4-Pyridoxic Acid 5-(Dihydrogen Phosphate) (I; X = CO_2H).—(a) *From the pyridil* (II). Hydrogen peroxide (1 ml. of 100-vol.) was added to the pyridil (II) (500 mg.) in 1·0N-sodium

[10] Ciamician and Silber, *Ber.*, 1909, **42**, 1386; Mascarelli, *Gazzetta*, 1906, **36**, II, 670.
[11] Terenin, *Acta Physicochim. U.R.S.S.*, 1940, **13**, 1.
[12] Dirscherl, *Z. physiol. Chem.*, 1930, **188**, 225.
[13] Davison, personal communication.

hydroxide (6 ml.). After 15 min. at room temperature 2N-hydrochloric acid (3 ml.) was added, to give 4-*pyridoxic acid* 5-(*dihydrogen phosphate*) which, recrystallised from water, had m. p. 203—205° (340 mg.) [Found: C, 37·1; H, 4·0; N, 5·4; P, 11·6%; equiv. (potentiometric titration), 94·6. $C_8H_{10}O_7NP$ requires C, 36·5; H, 3·8; N, 5·3; P, 11·7%; equiv., 94·6], $\lambda_{max.}$ 318 (ε 6720), $\lambda_{min.}$ 273—274 mμ (ε 1360) at pH 7·0.

(b) *From pyridoxamine* 5-(*dihydrogen phosphate*) (I; X = $CH_2{\cdot}NH_2$). Pyridoxamine phosphate (2·48 g.) was dissolved in 0·1N-sulphuric acid (50 ml.) and stirred with freshly precipitated manganese dioxide (10 g.). 10N-Sulphuric acid was added dropwise until the manganese dioxide had dissolved. The solution was kept at room temperature for 3 hr., the pH adjusted to 2·0 with sodium hydroxide, and the carboxylic acid filtered off and recrystallised (1·65 g.; m. p. 202—205°).

(c) *From pyridoxal* 5-(*dihydrogen phosphate*) (I; X = CHO). A solution of pyridoxal phosphate (2·65 g.) in 0·1N-sodium hydroxide (150 ml.) was exposed to a powerful ultraviolet lamp and a steady stream of oxygen was passed through it. After 6 hr. the peak at 388 mμ was replaced by one at 318—320 mμ. 2N-Hydrochloric acid (7·5 ml.) was added and, on concentration of the solution to *ca.* 50 ml., the pyridoxic acid phosphate (2·20 g.) crystallised; it had m. p. 201—205°.

Hydrolysis of 4-*Pyridoxic Acid* 5-(*Dihydrogen Phosphate*).—The phosphate (250 mg.) in concentrated aqueous hydrochloric acid (10 ml.) was boiled for 18 hr. under reflux. The solution was evaporated to dryness under reduced pressure and the residue treated with excess of saturated aqueous sodium hydrogen carbonate, whereupon the lactone of 4-carboxy-3-hydroxy-5-hydroxymethyl-2-methylpyridine was precipitated (135 mg.; m. p. 275—276°). This compound was identical with material prepared by the method of Heyl.[14]

Reduction of Pyridoxal 5-(*Dihydrogen Phosphate*) *with Sodium Borohydride*.—Sodium borohydride (500 mg.) was added to pyridoxal phosphate (530 mg.) in 0·5N-aqueous sodium hydroxide (10 ml.). When, after 5 min., the yellow solution had become colourless, its pH was adjusted to 5·0 with acetic acid and it was run on to a column of Amberlite XE 97 resin (2 × 30 cm.). The column was eluted with water and that fraction of the eluate absorbing ultraviolet light at 325 mμ was collected and evaporated to dryness under reduced pressure. The residue, freed from borate by repeated evaporation with methanol, was recrystallised from aqueous ethanol, to give pyridoxin 5-(dihydrogen phosphate) (310 mg.), m. p. 208—210°, identical with a sample made by deaminating pyridoxamine phosphate [1] (Found: C, 39·5; H, 5·0; N, 5·6; P, 12·4. Calc. for $C_8H_{12}O_6NP$: C, 38·5; H, 4·9; N, 5·6; P, 12·4%).

Reduction of the Pyridil (II) *with Sodium Borohydride*.—Sodium borohydride (500 mg.) was added to the pyridil (500 mg.) in 0·2N-sodium hydroxide (20 ml.). After 5 min. the mixture was worked up as in the previous experiment. Fractionation on XE 97 resin gave two fractions absorbing ultraviolet light at 325 mμ. They differed in the ease with which they could be freed from borate by evaporation with methanol, but once borate-free they had similar elementary analyses and behaved in the same way when oxidised with periodate (see below). Fraction A was eluted first. It was freed from borate by repeated evaporation with methanol, and the residue recrystallised from aqueous ethanol to give 5 : 5′-*bis*(*dihydroxyphosphinyloxymethyl*)-3 : 3′-*dihydroxy*-2 : 2′-*dimethyl*-4 : 4′-*hydropyridoin* (205 mg.), m. p. >300°. Fraction B was eluted from the column subsequently. After repeated evaporation with methanol (20 × 100 ml.), it was borate-free and recrystallised from aqueous ethanol to give the hydropyridoin (115 mg.), m. p. >300° [Found: (fraction A) C, 38·4; H, 4·4; N, 5·7; P, 13·1; (fraction B) C, 38·2; H, 4·3; N, 5·8; P, 12·9. $C_{16}H_{22}O_{12}N_2P_2$ requires C, 38·7; H, 4·5; N, 5·65; P, 12·5%).

Periodate Oxidations.—These were carried out with sodium metaperiodate in aqueous solution buffered to pH 4·0. The periodate remaining unconsumed after 4 hr. was estimated in the usual way by titrating, with standard arsenite, the iodine which it liberated from iodide. The products were examined by electrophoresis on filter paper (see below).

(*a*) Pyridoxal 5-(dihydrogen phosphate) used 0·15 mole of periodate per mole and gave small amounts of four products, the only one identified being 3 : 4-dihydroxy-2-methyl-5-pyridylmethyl dihydrogen phosphate (I; X = OH).

(*b*) The pyridil (II) used 1·0 mole of periodate per mole and gave 4-pyridoxic acid 5-(dihydrogen phosphate) (I; X = CO_2H) as the only product. From the pyridil (500 mg.), oxidised for 5 min. at room temperature with excess of sodium periodate, the crystalline carboxylic

[14] Heyl, *J. Amer. Chem. Soc.*, 1948, **70**, 3434.

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acid (485 mg.), m. p. 202—205°, was obtained by adjusting the pH of the reaction mixture to 2·0.

(*c*) The hydropyridoin used 1·2 moles of periodate per mole. The main product was pyridoxal 5-(dihydrogen phosphate) which was isolated, in aqueous solution, by elution from the paper after electrophoresis of the reaction mixture; its identity was confirmed by its ultraviolet absorption. Other products corresponding to the substances formed by oxidation of pyridoxal phosphate itself were also found by electrophoresis on filter paper.

Electrophoresis on Filter Paper.—Electrophoresis was carried out on Whatman 3 mm. filter paper with a 0·067M-phosphate buffer at pH 7·0. Voltages of 300 v were applied to the paper (12 × 40 cm.) for 4—6 hr. The compounds were seen most easily under ultraviolet light after light spraying with 5N-ammonia. Relative rates of travel were as tabulated.

Substance	Rate of travel to anode	Appearance of spot
Pyridoxal 5-(dihydrogen phosphate)	1·0	Yellow fluorescent
Pyridoxamine 5-(dihydrogen phosphate)	0·6	Blue fluorescent
4-Pyridoxic acid 5-(dihydrogen phosphate)	1·1	Bright white fluorescent
3 : 4-Dihydroxy-2-methyl-5-pyridylmethyl dihydrogen phosphate	0·75	Absorbent
Pyridoxal	−0·1	Yellow weak fluorescent
4-Pyridoxic lactone	0·2	Bright white fluorescent
Pyridil (II)	1·0	Yellow, absorbent
Pyridoxal phosphate oxime	0·85	Blue fluorescent
Oxime of the pyridil	0·85	Absorbent

ROCHE PRODUCTS LTD., WELWYN GARDEN CITY, HERTS. [*Received, August 21st*, 1957.]

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46. *The Mannans of Ivory Nut* (Phytelephas macrocarpa). *Part II.*[1] *The Partial Acid Hydrolysis of Mannans A and B.*

By G. O. ASPINALL, R. B. RASHBROOK, and (in part) G. KESSLER.

Partial acetolysis of mannan A, followed by deacetylation, afforded a homologous series of β-1 : 4-linked oligosaccharides (mannobiose to mannopentaose). Smaller quantities of mannose-containing oligosaccharides with some α-1 : 4-linkages, and of β-1 : 4-linked oligosaccharides containing both mannose and glucose residues were isolated. A similar series of oligosaccharides was isolated from mannan B. The significance of these results is discussed.

IT was shown in Part I [1] that ivory nut mannans A and B are both mixtures of at least two molecular species, terminated by D-mannopyranose and D-galactopyranose residues; both species are linear, but in addition to the dominant β-1 : 4-mannopyranosyl linkages, the evidence indicated the presence also of some mannose residues linked through $C_{(1)}$ and $C_{(6)}$. In order to obtain further information concerning the detailed molecular structure of these polysaccharides we have studied the products of partial acid hydrolysis.

Since the mannans are relatively insoluble in water, partial acid hydrolysis was most conveniently effected by acetolysis with a mixture of acetic anhydride, acetic acid, and sulphuric acid; the products thereof were deacetylated with barium methoxide, and the resulting mixtures were fractionated by chromatography on charcoal, followed where necessary by partition chromatography on cellulose. Thus mannan A afforded as the main products a homologous series of β-1 : 4-linked oligosaccharides composed solely of D-mannose residues. Mannobiose gave an identical *X*-ray powder photograph and had a similar melting point, but differed slightly in optical rotation from 4-*O*-β-D-mannopyranosyl-D-mannose (I; $n = 0$) isolated by Whistler and Stein from the partial acid hydrolysis of guaran.[2] The structure of the disaccharide was confirmed in studies of

[1] Part I, Aspinall, Hirst, Percival, and Williamson, *J.*, 1953, 3184.
[2] Whistler and Stein, *J. Amer. Chem. Soc.*, 1951, **73**, 4187.

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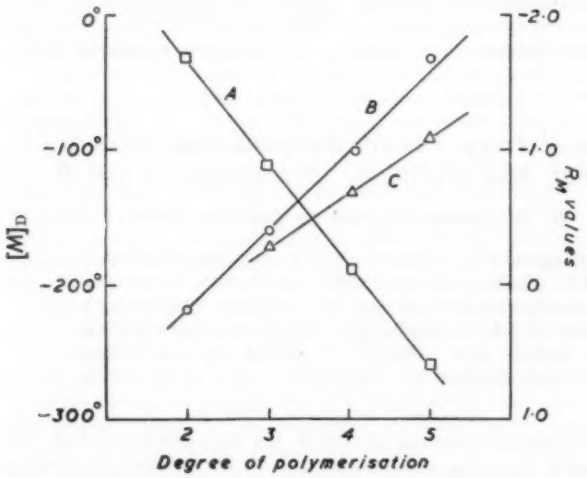
methylation and periodate oxidation. Mannotriose crystallised as the trihydrate and gave an identical *X*-ray powder photograph and had a similar melting point, but again differed slightly in optical rotation from the β-1 : 4-linked mannotriose (I; $n = 1$) previously isolated from the partial acid hydrolysis of guaran.[3] The derived mannotri-itol dodeca-acetate had similar physical constants to those quoted by Whistler and Smith.[3] Mannotetraose (I; $n = 2$) and mannopentaose (I; $n = 3$) were established as members of the same homologous series by the following observations: (i) the molecular rotations and the R_M values [4] of the sugars, mannobiose to mannopentaose, when plotted against degree of polymerisation gave straight line graphs (see Figure); (ii) chromatographic examination of the products of partial acid hydrolysis showed mannose and the lower homologues of the series.

(I) Man*p* 1$\overset{\beta}{\text{—}}$[—4 Man*p* 1$\overset{\beta}{\text{—}}$]$_n$—4 Man*p* Man*p* 1$\overset{\alpha}{\text{—}}$[—4 Man*p* 1$\overset{\beta}{\text{—}}$]$_n$—4 Man*p* (II)

Man*p* 1$\overset{\beta}{\text{—}}$[—4 Man*p* 1$\overset{\beta}{\text{—}}$]$_n$—4 Glu*p* (III)

Small quantities of two other series of oligosaccharides were also isolated; the first series contained only mannose residues, but in the second series each oligosaccharide



Molecular rotations and R_M *values of mannose-containing oligosaccharides plotted against degree of polymerisation.*

A, $[M]_D$ *values of ligosaccharides* (I). *B,* R_M *values of oligosaccharides* (I). *C,* R_M *values of oligosaccharides* (II).

contained mannose residues and one glucose residue per molecule. Disaccharide A gave only mannose on hydrolysis and had an optical rotation indicative of an α-glycosidic linkage. The following observations leave little doubt that this disaccharide is 4-*O*-α-D-mannopyranosyl-D-mannose (II; $n = 0$): (i) periodate oxidation [5] afforded formaldehyde, indicating the absence of a 1 : 5- or 1 : 6-linkage; (ii) reaction with phenylhydrazine gave a disaccharide phenylosazone, showing that a 1 : 2-linkage was not present; (iii) chromatography showed the presence of a tetrose (erythrose) when the disaccharide was oxidised with lead tetra-acetate under controlled conditions and the product hydrolysed,[6] indicating the presence of a 1 : 4-linked disaccharide (under similar conditions 1 : 3-linked hexose-containing disaccharides yield pentoses). Confirmation of the presence of the α-1 : 4-linkage in the disaccharide came from experiments carried out on trisaccharide C.

[3] Whistler and Smith, *J. Amer. Chem. Soc.*, 1952, **74**, 3795.
[4] Bate-Smith and Westhall, *Biochem. Biophys. Acta*, 1950, **4**, 427.
[5] Reeves, *J. Amer. Chem. Soc.*, 1941, **63**, 1476.
[6] Perlin, *Analyt. Chem.*, 1955, **27**, 396.

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Hydrolysis of the crystalline trisaccharide gave only mannose, and partial acid hydrolysis gave both mannobioses and mannose, but partial acid hydrolysis of the derived glycitol (potassium borohydride reduction) gave only the α-linked mannobiose and mannose. When oxidised with periodate the quantity of reagent consumed by the trisaccharide was exactly parallel to the quantity consumed by the β-linked mannotriose (I; $n = 1$), suggesting the presence of similar linkages in the two trisaccharides. The optical rotation of trisaccharide C was consistent with the presence of one α-linked and one β-linked D-mannopyranosyl residue. Proof that the non-reducing end-group (with the α-configuration) was glycosidically linked to position 4 of the central mannose unit in the trisaccharide came from the isolation of 2 : 3 : 4 : 6-tetra- and 2 : 3 : 6-tri-*O*-methyl-D-mannose from the hydrolysis of the methylated glycitol. Trisaccharide C is, therefore, *O*-α-D-mannopyranosyl-(1 → 4)-*O*-β-D-mannopyranosyl-(1 ← 4)-D-mannopyranose (II; $n = 1$). Small quantities of a second tetrasaccharide and a second pentasaccharide were also isolated. It is probable from chromatographic examination of the oligosaccharides and their partial hydrolysis products that these belong to the same homologous series (II; $n = 2$ and 3).

The glucose-containing oligosaccharides were not isolated in sufficient quantity for complete characterisations to be carried out. The following observations, however, suggest that the disaccharide B is probably 4-*O*-β-D-mannopyranosyl-D-glucose (III; $n = 0$): (i) hydrolysis of the disaccharide gave glucose and mannose, but hydrolysis of the derived aldobionic acid (bromine oxidation) gave only mannose; (ii) the optical rotation indicated that the mannosylglucose was β-linked; (iii) periodate oxidation [5] afforded formaldehyde, indicating the absence of a 1 : 5- or 1 : 6-linkage; (iv) reaction with phenylhydrazine gave a disaccharide phenylosazone, showing that a 1 : 2-linkage was not present; (v) controlled oxidation of the disaccharide with lead tetra-acetate followed by hydrolysis of the oxidation product gave erythrose, pointing to a 1 : 4-linkage. Since the phenylosazone of disaccharide B was different from that derived from β-1 : 4-linked mannobiose (I; $n = 0$), there is still doubt concerning the structure of the disaccharide. Trisaccharide D, which gave on hydrolysis mannose and glucose in the approximate ratio of 2 : 1, had an optical rotation indicative of β-linkages. Partial acid hydrolysis of the trisaccharide gave mannose, glucose, mannobiose (I; $n = 0$), and disaccharide A, but on hydrolysis of the derived glycitol only mannose and mannobiose could be detected. Subject to the same reservations as in the case of disaccharide B, the trisaccharide probably belongs to the same homologous series (III; $n = 1$).

The partial acid hydrolysis of mannan B afforded a similar series of oligosaccharides. Again, the major products were the β-1 : 4-linked oligosaccharides (I; $n = 0$, 1, and 2), which were isolated as the crystalline sugars. The other oligosaccharides (II; $n = 0$ and 1) and (III; $n = 0$ and 1) which had been isolated from mannan A were identified chromatographically.

These results provide additional evidence for the presence in the ivory nut mannans of chains of 1 : 4-linked β-D-mannopyranosyl units, and again show that there are no essential structural differences between mannans A and B. The presence, however, of a small proportion of α-linked D-mannose units was not previously suspected. From the present evidence it is probable that the α-linked oligosaccharides are of structural significance and are not artefacts, since control experiments provided no evidence for their formation either from mannose by reversion or from the β-linked oligosaccharides by acid-catalysed anomerisation at the glycosidic bond.[7] It is not yet possible to assess the structural significance of the glucose-containing oligosaccharides. Although the ivory nut mannans contain a small proportion of glucose residues so that partial hydrolysis should give rise to some glucose-containing oligosaccharides, these substances may have been formed by epimerisation of the mannose-containing oligosaccharides. No further evidence was found to confirm the presence in the mannans of 1 : 6-linkages.[1]

[7] Cf. Lindberg, *Acta Chem. Scand.*, 1949, **3**, 1153.

Experimental

Paper partition chromatography was carried out on Whatman No. 1 filter paper with the following solvent systems (v/v): (A) ethyl acetate–pyridine–water (10 : 4 : 3); (B) butan-1-ol–ethanol–water (4 : 1 : 5, upper layer); (C) butan-2-one saturated with water; (D) ethyl acetate–propan-2-ol–water (16 : 10 : 5).

Mannan A was prepared by extraction of delignified ivory nut shavings with 7% aqueous potassium hydroxide as described previously.[1] The polysaccharide, which had $[\alpha]_D^{18}$ −48° (*c* 1·1 in N-NaOH), was used without further purification. Mannan B was prepared as described previously [1] and had $[\alpha]_D^{18}$ −26° (*c* 1·0 in anhydrous formic acid).

Acetolysis of Mannan A and Fractionation of Derived Oligosaccharides.—Mannan A (55 g.) was added slowly with stirring to a mixture of acetic anhydride (330 ml.), glacial acetic acid (330 ml.), and concentrated sulphuric acid (33 ml.) at 0°. The mixture was kept at room temperature for 72 hr., during which the mannan had completely dissolved (*ca.* 36 hr.). The mixture was filtered, then poured slowly with stirring into ice-water, and sodium hydrogen carbonate was added gradually (to pH 3—4). The precipitated sugar acetates were filtered off, and the filtrate was extracted with chloroform (3 × 800 ml.). The solid acetates were dissolved in chloroform, the solution was combined with the chloroform extracts, and the combined solutions were washed with sodium hydrogen carbonate solution, dried, and concentrated. A solution of barium methoxide (7·5 g.) in methanol (75 ml.) was added to a solution of the sugar acetates (90·7 g.) in chloroform (250 ml.) and methanol (500 ml.) at 0°, and the mixture was shaken for 1 hr. and set aside overnight at 0°. The mixture was exactly neutralised by the addition of dilute sulphuric acid, and water (175 ml.) was added. The chloroform layer was separated, and the aqueous layer was filtered through a pad of " Celite " and concentrated. The mixture of sugars (45·8 g.), dissolved in water (200 ml.), was added to a column of charcoal–Celite (1·3 kg.; 2 : 1). Elution with water and water containing 0·5—4·0% of ethanol yielded a mixture of monosaccharides (mannose, together with small quantities of xylose, glucose, and galactose) (6·5 g.) which was not examined further. Oligosaccharides were eluted with ethanol–water containing increasing proportions of ethanol and eight fractions were collected.

Examination of Oligosaccharide-containing Fractions.—Fraction 1. The sugar (9·8 g.; eluted with water containing 4·5—6·5% of ethanol) was crystallised from ethanol–water and had $R_{mannose}$ 0·52 in solvent A, m. p. 202—203°, and $[\alpha]_D^{19}$ −5·2° ⟶ −8·5° (2 hr., const.) (*c* 5·4 in H_2O). Whistler and Stein [2] report m. p. 193·5—194° and $[\alpha]_D^{25}$ −7·7° ⟶ −2·2° (equil.) (in H_2O) for 4-*O*-β-D-mannopyranosyl-D-mannopyranose, but the two samples gave identical *X*-ray powder photographs (comparison kindly undertaken by Professor R. L. Whistler). Treatment of a sample of the sugar with sodium metaperiodate solution [3] resulted in the consumption of 4·0 mol. of reagent after 48 hr., followed the consumption of a fifth mol. after 120 hr.; further reaction occurred slowly thereafter. On reaction with potassium metaperiodate [3] 3 mol. of formic acid were released after 185 hr., but no definite break in reaction occurred at this point. A sample (*ca.* 1 g.) of the sugar was methylated successively with methyl sulphate and sodium hydroxide, and methyl iodide and silver oxide, to yield the fully methylated disaccharide (310 mg.). A portion of the methylated sugar (100 mg.) was hydrolysed by N-sulphuric acid in a sealed tube at 100° for 6 hr. After neutralisation with barium carbonate, the hydrolysate was separated on filter sheets (Whatman 3MM), with solvent B, to give fractions *a* (35 mg.; R_G 1·0) and *b* (25 mg.; R_G 0·80). These sugars were identified as 2 : 3 : 4 : 6-tetra- and 2 : 3 : 6-tri-*O*-methyl-D-mannose by conversion into their respective aniline derivatives, m. p. and mixed m. p. 141—143° and 120·5—123°. On reaction with phenylhydrazine 4-*O*-β-D-mannopyranosyl-D-mannose gave a phenylosazone, which crystallised in spherulitic aggregates of needles and had m. p. 203—206° (Found: *M*, 526, by absorption [3] at 396 mμ).

Fraction 2. The syrup (1·28 g.; eluted with water containing 6·5—8·0% of ethanol) contained three components, 4-*O*-β-D-mannopyranosyl-D-mannose, and disaccharides A and B, having $R_{mannose}$ 0·52, 0·62, and 0·38. Chromatographically pure samples of disaccharides were obtained by successive fractionations on columns of powdered cellulose and on filter sheets with solvent D.

Disaccharide A had $[\alpha]_D^{17}$ +49° (*c* 0·6 in H_2O) and gave only mannose on hydrolysis. Periodate oxidation of the disaccharide in sodium hydrogen carbonate buffer [3] afforded formaldehyde, identified as the dimedon derivative, m. p. and mixed m. p. 187—190° (under

[1] Halsall, Hirst, and Jones, *J.*, 1947, 1399, 1427.
[3] Barry, McCormick, and Mitchell, *J.*, 1955, 222.

similar conditions no formaldehyde was formed from gentiobiose). A sample of the disaccharide (*ca.* 1 mg.) was dissolved in water (0·01 ml.) and glacial acetic acid (0·09 ml.), and lead tetra-acetate (5 mg.) in glacial acetic acid (0·4 ml.) was added. After 2 hr. excess of oxalic acid was added, and the solution was diluted with water and heated on the water-bath with Amberlite resin IR-120(H). Chromatographic examination of the hydrolysate showed erythrose but no arabinose (under similar conditions laminaribiose afforded arabinose). On reaction with phenylhydrazine the disaccharide gave a phenylosazone, m. p. 200—201° (Found: *M*, 600, by absorption [9] at 396 mμ).

Disaccharide B had $[\alpha]_D^{17}$ +5·5° (*c* 3·5 in H_2O) and gave mannose and glucose on hydrolysis. Hydrolysis of the derived aldonic acid gave only mannose. Periodate oxidation of the disaccharide in sodium hydrogen carbonate buffer [5] afforded formaldehyde, identified as the dimedon derivative, m. p. and mixed m. p. 187—190°. Lead tetra-acetate oxidation of the disaccharide followed by chromatographic examination of the hydrolysate gave erythrose but no arabinose. On reaction with phenylhydrazine the disaccharide gave a phenylosazone, m. p. 149—152° (Found: *M*, 542, by absorption at 396 mμ), which crystallised in leaflets and gave an *X*-ray powder photograph different from that of the phenylosazone from 4-*O*-β-D-mannopyranosyl-D-mannose.

Fraction 3. The sugar (5·6 g.; eluted with water containing 9·0—10·0% of ethanol) was crystallised from ethanol–water and had $R_{mannose}$ 0·22 in solvent A, m. p. (rapid heating) 134·5—135·5°, and $[\alpha]_D^{17}$ −15·7° ⟶ −20·2° (equil.) (*c* 1·29 in H_2O) (Found: C, 39·0; H, 7·1. Calc. for $C_{18}H_{32}O_{16},3H_2O$: C, 38·7; H, 6·9%). Whistler and Smith report m. p. 137—137·5° and $[\alpha]_D^{25}$ −24·7° ⟶ −23·3° for *O*-β-D-mannopyranosyl-(1 ⟶ 4)-*O*-β-D-mannopyranosyl-(1 ⟶ 4)-D-mannopyranose trihydrate, but the two samples gave identical *X*-ray powder photographs (comparison kindly undertaken by Professor R. L. Whistler). On slow heating on the Kofler hot-stage the sugar had m. p. 166·5—169·5° (presumably that of the anhydrous form); Dr. L. Hough [10] reports a similar observation. The sugar (300 mg.) was dissolved in water (6 ml.), and a solution of potassium borohydride (100 mg.) in water (2 ml.) was added. After 45 min. excess of borohydride was destroyed by the addition of dilute acetic acid, and the solution was taken to dryness. The residue was heated at 100° for 30 min. with acetic anhydride (12 ml.) and anhydrous sodium acetate (150 mg.). The solution was poured into ice-water; the precipitate after recrystallisation from ethanol–light petroleum (b. p. 80—100°) and from ethanol had m. p. 112·5—115° and $[\alpha]_D^{18}$ −24° (*c* 2·0 in $CHCl_3$) {Whistler and Smith [3] report m. p. 113·5—114° and $[\alpha]_D^{25}$ −21° (in $CHCl_3$) for mannotri-itol dodeca-acetate}.

Fraction 4. The syrup (1·84 g.; eluted with water containing 10·5—11·5% of ethanol) contained three components, mannotriose, and trisaccharides C and D, having $R_{mannose}$ 0·22, 0·29, and 0·15 respectively. Chromatographically pure samples of trisaccharides C and D were obtained after fractionation on cellulose with solvent C. Trisaccharide C crystallised from ethanol–water and had m. p. 224—225° and $[\alpha]_D^{18}$ +43° (5 min.) ⟶ +40° (1 hr., const.) (*c* 2·1 in H_2O) (Found: C, 42·9; H, 6·4. $C_{18}H_{32}O_{16}$ requires C, 42·8; H, 6·4%). Partial acid hydrolysis of the trisaccharide yielded mannose, mannobiose, and disaccharide A; partial acid hydrolysis of the derived glycitol (borohydride reduction) gave mannose and disaccharide A. When oxidised with periodate [11] the trisaccharide consumed 5·0 mol. after 8 hr. and 6·0 mol. after 24 hr.; *O*-β-D-mannopyranosyl-(1 ⟶ 4)-*O*-β-D-mannopyranosyl)-(1 ⟶ 4)-D-mannopyranose trihydrate consumed 5·0 ml. after 8 hr. and 5·95 mol. after 24 hr. Trisaccharide C (100 mg.) was dissolved in water (4 ml.) and a solution of potassium borohydride (40 mg.) in water (1 ml.) was added. The reaction mixture was kept at room temperature for 1 hr., excess of borohydride was destroyed by the addition of acetic acid, and inorganic salts were removed by passage through columns of Amberlite resins IR-100(H) and IR-4B(OH). The reduction product was methylated by successive additions of methyl sulphate and sodium hydroxide. The methylated glycitol (*ca.* 120 mg.), isolated from the mixture by chloroform extraction, was hydrolysed by 0·5N-sulphuric acid (10 ml.) for 3 hr. at 100°, and the hydrolysate was neutralised with barium carbonate, deionised, and concentrated. Separation of the reducing sugars in the hydrolysate on filter sheets with solvent C gave fractions *a* (42 mg.) and *b* (31 mg.). Fraction *a* was identified as 2 : 3 : 4 : 6-tetra-*O*-methyl-D-mannose by conversion into the aniline derivative, m. p. and mixed m. p. 142—144°. Fraction *b* was identified as 2 : 3 : 6-tri-*O*-methyl-D-mannose by conversion into the di-*p*-nitrobenzoate, m. p. and mixed m. p. 183—185°.

[10] Dr. L. Hough, personal communication.
[11] Aspinall and Ferrier, *Chem. and Ind.*, 1957, 1216.

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Trisaccharide D had $[\alpha]_D^{17}$ −7·0° (*c* 4·1 in H_2O) and gave on hydrolysis mannose and glucose in the approximate ratio of 2 : 1. Partial acid hydrolysis of the trisaccharide yielded mannose, glucose, mannobiose, and disaccharide B; partial acid hydrolysis of the derived glycitol gave mannose and mannobiose.

Fraction 5. The sugar (2·1 g.; eluted with water containing 11·5—13·0% of ethanol) crystallised from ethanol–water, and after several recrystallisations had $R_{mannose}$ 0·11 in solvent A, m. p. 231·5—232°, and $[\alpha]_D^{20}$ −31·6° (5 min.) ⟶ −28·7° (50 min., const.) (*c* 0·9 in H_2O). The sugar gave only mannose on hydrolysis and after partial acid hydrolysis chromatography showed the homologous series, mannose, mannobiose, mannotriose, and unchanged tetrasaccharide.

Fraction 6. The syrup (0·9 g.; eluted with water containing 13·0—14·5% of ethanol) contained mannotetraose together with samll quantities of a faster-moving component ($R_{mannose}$ 0·17). The minor component, separated on filter sheets with solvent A, gave only mannose on hydrolysis, and on partial acid hydrolysis mannose, mannobiose, mannotriose, disaccharide A, and trisaccharide C could be detected by chromatography.

Fraction 7. The sugar (0·9 g.; eluted with water containing 15—16% of ethanol) crystallised from ethanol–water and had $[\alpha]_D^{20}$ −30·2° (*c* 2·1 in H_2O); no m. p. (>280°) could be recorded. On partial acid hydrolysis, the homologous series of oligosaccharides, mannose, mannobiose, mannotriose, mannotetraose, and unchanged pentasaccharide were detected chromatographically.

Fraction 8. The syrup (0·8 g.; eluted with water containing 17—18% of ethanol) contained a complex mixture of oligosaccharides including a component having $R_{mannose}$ 0·08. A small quantity of this sugar was separated on filter sheets with solvent A and yielded on partial acid hydrolysis mannose, mannobiose, mannotriose, disaccharide A, and trisaccharide C.

Acetolysis of Mannan B and Fractionation of Derived Oligosaccharides.—Mannan B (13 g.) was added slowly to a mixture of acetic anhydride (80 ml.), glacial acetic acid (80 ml.), and concentrated sulphuric acid (8 ml.) at 0°. After 96 hr. at room temperature, the mixture was poured into ice-water (750 ml.), and sodium hydrogen carbonate was added slowly (to pH 3—4). The precipitated sugar acetates were filtered off and dissolved in chloroform, and the solution was combined with a chloroform extract (3 × 500 ml.) of the aqueous filtrate. The chloroform solution was washed with aqueous sodium hydrogen carbonate, dried (Na_2SO_4), and concentrated to give a mixture of sugar acetates (14·6 g.). A portion of the sugar acetates (10·1 g.) was dissolved in dry methanol (150 ml.), and a solution of barium methoxide (1·35 g.) in methanol (15 ml.) was added. The mixture was shaken for 1 hr. and set aside at 0°. The mixture was worked up as described previously for mannan A and yielded a mixture of sugars (4·8 g.). The mixture of sugars dissolved in water (150 ml.) was added to a column of charcoal–Celite (300 g.; 1 : 1). Elution with water and ethanol–water (2 : 98) gave a mixture of monosaccharides (mannose, together with traces of xylose, glucose, and galactose; 0·42 g.) which was not examined further. Oligosaccharides were eluted with ethanol–water containing increasing proportions of ethanol. Elution with water containing 4—6% of ethanol gave 4-*O*-β-D-mannopyranosyl-D-mannopyranose (0·92 g.), m. p. and mixed m. p. 203—206°, which gave an *X*-ray powder photograph identical with that of an authentic sample. Elution with water containing 7—8% of ethanol yielded a syrup (84 mg.) shown by chromatography to contain three disaccharides (mannobiose, and disaccharides A and B) having $R_{mannose}$ 0·52, 0·62, and 0·38 in solvent A. Elution with water containing 9% of ethanol gave mannotriose trihydrate (600 mg.), which, after recrystallisation from ethanol–water, had m. p. and mixed m. p. 134·5—135·5°, and gave an *X*-ray powder identical with that of an authentic sample. Elution with water containing 10—11% of ethanol gave a mixture (166 mg.) of mannotriose, and trisaccharides C and D having $R_{mannose}$ 0·22, 0·29, and 0·15. Elution with water containing 12% of ethanol afforded mannotetraose, which, after recrystallisation from ethanol–water, had m. p. and mixed m. p. 231·5—232° and gave an *X*-ray powder photograph identical with that of an authentic sample.

Tests for Acid Reversion during Acetolysis.—Samples of mannose, mannobiose, and mannotriose (150—200 mg.) were each dissolved in 2 ml. of acetolysis mixture [acetic anhydride, acetic acid, and concentrated sulphuric acid, 10 : 10 : 1 (v/v)] at 0°. The solutions were kept at room temperature for 48 hr., filtered, and poured into ice-water, and sodium hydrogen carbonate solution was added. The sugar acetates, isolated by chloroform extraction, were deacetylated with barium methoxide in methanol at 0° for 18 hr., and the mixture was poured

into water. The resulting solution was deionised by passage through columns of Amberlite resins IR-120(H) and IR-4B(OH) and by electrodialysis with ion-exchange membranes,[12] and concentrated. Chromatographic examination of the products in solvent A showed only starting materials and hydrolysis products.

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DEPARTMENT OF CHEMISTRY, UNIVERSITY OF EDINBURGH. [*Received, August 23rd*, 1957.]

[12] Anderson and Wylam, *Chem. and Ind.*, 1956, 191.

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47. *Gum Ghatti (Indian Gum). Part II.* The Hydrolysis Products obtained from the Methylated Degraded Gum and the Methylated Gum.*

By G. O. ASPINALL, (MRS.) BARBARA J. AURET, and E. L. HIRST.

Hydrolysis of methylated degraded gum ghatti yields 2 : 3 : 4 : 6-tetra-, 2 : 3 : 4-tri-, 2 : 3-, and 2 : 4-di-*O*-methyl-D-galactose, 3 : 4 : 6-tri-*O*-methyl-D-mannose, and 2 : 3 : 4-tri-*O*-methyl-D-glucuronic acid, together with traces of other sugars. Hydrolysis of methylated gum ghatti affords 2 : 3 : 5-tri-, 2 : 3-, 2 : 4-, 2 : 5-, and 3 : 5-di-*O*-methyl-L-arabinose, 2 : 3 : 4 : 6-tetra-, 2 : 3 : 4-tri-, 2 : 4-di-, and 2-mono-*O*-methyl-D-galactose, 4-*O*-methyl-D-mannose, 2 : 3 : 4-tri-*O*-methyl-L-rhamnose, 2 : 3 : 4-tri-, and 2 : 3-di-*O*-methyl-D-glucuronic acid, together with traces of other sugars. Partial structures for the gum are discussed in the light of these and previous results.

IT was shown in Part I that gum ghatti (Indian gum) from *Anogeissus latifolia*, Wall, is composed of the following sugar residues, L-arabinose (5 parts), D-galactose (3 parts), D-mannose (1 part), and D-glucuronic acid (1 part), together with the small amounts of xylose and a 6-deoxyhexose (probably rhamnose). Most of the arabinose residues are located in the outer parts of the molecular structure since autohydrolysis of the gum acid leads to the removal of these residues and the formation of a degraded gum, in which only a small proportion of arabinose residues are attached to the more resistant backbone of galactose, mannose, and glucuronic acid residues. Further hydrolysis of the gum under more drastic conditions gives D-galactose and a mixture of two aldobiouronic acids, characterised as 6-*O*-β-D-glucuronosyl-D-galactose and 2-*O*-β-D-glucuronosyl-D-mannose. An examination of the methylated sugars formed on hydrolysis of the methylated gum and the methylated degraded gum is now reported, and partial structures for the gum are discussed.

A sample of degraded gum ghatti (substantially arabinose-free), prepared by autohydrolysis of the gum acid, was converted into its fully methylated derivative. The methylated polysaccharide was hydrolysed, and the hydrolysate (containing acidic components as barium salts) was separated into an ether-soluble fraction and an ether-insoluble residue. The neutral methylated sugars present in the ether-soluble fraction were fractionated chromatographically on cellulose,[1] giving 2 : 3 : 4 : 6-tetra-*O*-methyl-, 2 : 3 : 4-tri-*O*-methyl-, 2 : 3- and 2 : 4-di-*O*-methyl-D-galactose, all of which were characterised as crystalline derivatives. Although no methyl ethers of D-mannose could be isolated in pure form and identified as crystalline derivatives, the presence of 3 : 4 : 6-tri-*O*-methylmannose was established by chromatography, paper ionophoresis, the detection of 2 : 3 : 5-tri-*O*-methylarabinose when a fraction containing the sugar was oxidised with periodate,[2] and the observation that a fraction containing the sugar in

* The paper by Aspinall, Hirst, and Wickstrøm (*J.*, 1955, 1160) is to be regarded as Part I.

[1] Hough, Jones, and Wadman, *J.*, 1949, 2511.

[2] Lemieux and Bauer, *Canad. J. Chem.*, 1953, **31**, 814.

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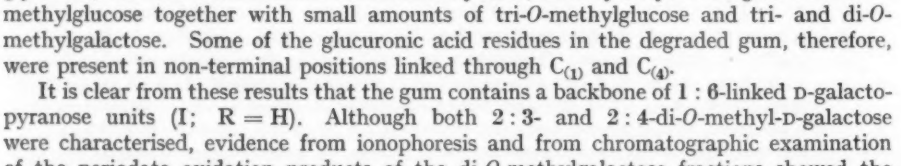
admixture with tetra- and 2 : 3 : 4-tri-*O*-methylgalactose was converted into the corresponding mixture of aldonamides, which gave a positive Weerman test. This sugar was the most important mannose derivative present, although traces of a di-*O*-methyl- (probably 3 : 4-) and 4-*O*-methyl-mannose were also observed. In addition, traces of 2 : 3 : 5-tri-*O*-methylarabinose and 2 : 3 : 4-tri-*O*-methyl-xylose and -rhamnose were detected chromatographically, but in insufficient quantity to be of structural significance. The ether-insoluble residue afforded further quantities of 2 : 3 : 4-tri- and di-*O*-methylgalactose, which were separated from the barium salts on filter sheets. The acidic fraction, consisting mainly of methylated aldobiouronic acids, was submitted to further acid hydrolysis under vigorous conditions, and again the acidic were separated from the neutral sugars. The neutral fraction contained 2 : 3 : 4-tri-*O*-methyl-D-galactose, identified as the aniline derivative, and 3 : 4 : 6-tri-*O*-methylmannose and 2 : 3-di-*O*-methylgalactose were identified chromatographically. The main component of the acidic fraction was identified chromatographically as 2 : 3 : 4-tri-*O*-methylglucuronic acid, and, after reduction of the methyl ester methyl glycoside and hydrolysis, as 2 : 3 : 4-tri-*O*-methylglucose. The minor component of the acidic fraction was converted into the methyl ester methyl glycoside, reduced with lithium aluminium hydride, and hydrolysed to give 2 : 3-di-*O*-methylglucose together with small amounts of tri-*O*-methylglucose and tri- and di-*O*-methylgalactose. Some of the glucuronic acid residues in the degraded gum, therefore, were present in non-terminal positions linked through $C_{(1)}$ and $C_{(4)}$.

It is clear from these results that the gum contains a backbone of 1 : 6-linked D-galactopyranose units (I; R = H). Although both 2 : 3- and 2 : 4-di-*O*-methyl-D-galactose were characterised, evidence from ionophoresis and from chromatographic examination of the periodate oxidation products of the di-*O*-methylgalactose fractions showed the 2 : 3-dimethyl ether to be the main component of the mixture. (When mixtures of these two sugars are present, the 2 : 4-dimethyl ether is more readily characterised as the relatively insoluble aniline derivative.) It follows that the main branching point in the degraded gum is through position 4 of galactose, although some small proportion of branching may also occur through position 3. Since the main products of hydrolysis of the methylated aldobiouronic acids were 2 : 3 : 4-tri-*O*-methylglucuronic acid, 2 : 3 : 4-tri-*O*-methylgalactose, and 3 : 4 : 6-tri-*O*-methylmannose, the aldobiouronic acid groups are



present as terminal groups (II and III; R = H). These groups are, therefore, attached as side-chains probably through position 4 of galactose residues in the backbone. At present, there is no indication whether these units are attached directly to the backbone or whether 1 : 6-linked galactose residues are interposed. The structural significance of the non-reducing D-galactopyranose end groups in the degraded gum is not yet clear. Although these end groups may terminate another type of side-chain, it is also possible that they are present at the non-reducing end of the backbone and arise from scission of the main chain during the autohydrolysis.

Fully methylated gum ghatti was hydrolysed, and the hydrolysate (containing acidic

components as barium salts) was separated into an ether-soluble fraction (A) and an ether-insoluble residue (B). The residue (B) was then separated by chromatography on cellulose to give neutral sugars (C), a pure sample of 2-*O*-methyl-D-galactose, and an acidic fraction. The combined neutral sugars (A) + (C) were chromatographed on cellulose, giving pure samples of most of the major components and mixtures containing the minor components, which were refractionated. The following methylated sugars were characterised as crystalline derivatives: 2 : 3 : 5-tri-, 2 : 3-, 2: 4-, 2 : 5-, and 3 : 5-di-*O*-methyl-L-arabinose, 2 : 3 : 4 : 6-tetra-, 2 : 3 : 4-tri-, 2 : 4-di-, and 2-mono-*O*-methyl-D-galactose, 4-*O*-methyl-D-mannose, and 2 : 3 : 4-tri-*O*-methyl-L-rhamnose. Traces of some other sugars were detected chromatographically, but these were present in insufficient amount to be of structural significance. The acidic fraction, which was contaminated by a small amount of 2-*O*-methylgalactose, was converted into the corresponding mixture of methyl ester methyl glycosides, which was reduced with lithium aluminium hydride and hydrolysed to give a mixture of neutral sugars. The methylated sugars were fractionated on cellulose, and the following sugars were identified as crystalline derivatives: 2 : 3 : 4-tri- and 2 : 3-di-*O*-methyl-D-glucose, 2 : 4-di- and 2-mono-*O*-methyl-D-galactose, and 4-*O*-methyl-D-mannose. The isolation of 2 : 3 : 4-tri- and 2 : 3-di-*O*-methyl-D-glucose indicates the presence in the methylated gum of residues of 2 : 3 : 4-tri- and 2 : 3-di-*O*-methyl-D-glucuronic acid. 2 : 4-Di-*O*-methyl-D-galactose and 4-*O*-methyl-D-mannose are the main neutral fragments arising from the aldobiouronic acid groupings. It is probable that the 2-*O*-methyl-D-galactose arose entirely from the contaminating neutral sugar and not from hydrolysis of a partially methylated aldobiouronic acid. In addition, a trace of 2 : 3 : 4-tri-*O*-methylgalactose was detected chromatographically

In view of the several stages involved in the separation and identification of the many methylated sugars formed on hydrolysis of the methylated gum, it is not possible to give more than an approximate estimate of the proportions of some of the constituent sugars arising from the neutral part of the gum. Since even more operations were involved in the identification of the acidic residues and of the neutral sugar residues attached thereto, and since the hydrolyses of acidic polysaccharides are usually accompanied by some decomposition, it is again only possible to estimate their relative proportions approximately. The significance of these results, taken together with previous results, may be assessed most conveniently by considering, in turn, the L-arabinose residues removed during the autohydrolysis, the backbone of 1 : 6-linked D-galactopyranose residues, and the aldobiouronic acid units. The approximate composition of the gum determined in Part I and expressed as parts per equivalent weight of gum acid provides a useful working model.

The quantity of 2 : 3 : 5-tri-*O*-methyl-L-arabinose isolated from the methylated gum accounts for approximately four of the five parts of L-arabinose present per equivalent of gum. Although relatively small amounts of 2 : 3 : 4-tri-*O*-methyl-L-rhamnose, 2 : 3 : 4 : 6-tetra-*O*-methyl-D-galactose, and 2 : 3 : 4-tri-*O*-methyl-D-glucuronic acid were also present as units of the methylated gum, terminal L-arabofuranose residues account for most of the non-reducing end groups in the gum. The fifth part of L-arabinose is accounted for by approximately equal amounts of 2 : 3-, 2 : 4-, 2 : 5-, and 3 : 5-di-*O*-methyl-L-arabinose. Three of these four sugars represent units not susceptible to attack by periodate. Since it was shown in Part I that about 20% of the arabinose residues in the gum are not attacked by periodate, it follows that most, if not all, of these sugars are of structural significance and do not arise from incomplete methylation of the gum or from demethylation during hydrolysis. These non-terminal arabinose residues must also occur in the outer parts of the molecule since they are removed as free arabinose during the autohydrolysis of the gum acid. It is clear, therefore, that the majority of L-arabinose residues in the gum occur in the furanose form as single-unit side-chains attached to the more resistant part of the structure. In a few cases, however, non-terminal L-arabinose residues must be interposed between the end groups and the other sugar residues. The small proportion of L-arabopyranose residues in the gum, as shown by the isolation of 2 : 4-di-*O*-methyl-L-arabinose,

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is of particular interest as until recently[3] L-arabinose had been found in combination only in the furanose form.

The D-galactose residues present in the gum occur in three main types of combination as shown by the isolation of 2 : 3 : 4-tri- (<1 part), 2 : 4-di- (>1 part), and 2-mono- (>1 part) *O*-methyl-D-galactose from the methylated gum. Since the corresponding residues in the methylated degraded gum afford 2 : 3 : 4-tri- and 2 : 3-di-*O*-methyl-D-galactose, it follows that the preferred mode of attachment of arabinose is to position 3 of galactose, although it is possible that some arabinose residues may also be linked to position 4. It is probable, however, that most of the 2-*O*-methyl-D-galactose represents a double branching point, to arabinose through position 3, and to aldobiuronic acid through position 4. These results are in reasonable agreement with the results of periodate oxidation of the gum (Part I) where it was shown that about a third of the galactose residues in the gum were attacked by periodate. There is no evidence at present as to the rôle of the very small proportion of D-galactopyranose end groups.

The sugar residues present in the aldobiouronic acid groupings in the methylated gum are those of 2 : 3 : 4-tri-*O*-methyl-D-glucuronic acid, 2 : 3-di-*O*-methyl-D-glucuronic acid (main acid component), 2 : 4-di-*O*-methyl-D-galactose, and 4-*O*-methyl-D-mannose, whereas the corresponding residues in the methylated degraded gum are those of 2 : 3 : 4-tri-*O*-methyl-D-glucuronic acid (main acid component), 2 : 3-di-*O*-methyl-D-glucuronic acid, 2 : 3 : 4-tri-*O*-methyl-D-galactose, and 3 : 4 : 6-tri-*O*-methyl-D-mannose. It follows that arabinose residues are attached to these sugars through position 3 of galactose, positions 3 and 6 of mannose, and through position 4 of some glucuronic acid residues. Apart from chromatographic and ionophoretic evidence for traces of 3 : 4 : 6-tri-*O*-methylmannose, the only derivative of D-mannose found in the hydrolysate from the methylated gum was the 4-methyl ether, indicating one main mode of linkage of mannose residues in the gum. The evidence adduced in Part I indicated, on the one hand, the presence of one part of mannose and one part of glucuronic acid per equivalent of gum, and, on the other hand, the linking of glucuronic acid to both galactose and mannose, and suggested that some mannose residues in the gum may be linked to neutral sugar residues only. Experiments to provide further evidence on this point are in progress.

In Part I it was shown that hydrolysis of gum ghatti affords small amounts of xylose and a 6-deoxyhexose (probably rhamnose) in addition to the main constituent sugars. The isolation of 2 : 3 : 4-tri-*O*-methyl-L-rhamnose from the methylated gum confirms the presence of L-rhamnose residues in the gum. No other methyl ethers of rhamnose were detected. Since this sugar has persisted throughout the various operations it seems probable that it is an integral part of the gum structure and does not arise from a contaminating polysaccharide. On the other hand, only traces of xylose derivatives (as the 2 : 3 : 4-trimethyl ether) could be detected on hydrolysis of the methylated gum. It is unlikely, therefore, that xylose is a constituent of the gum itself.

Our present knowledge of the detailed molecular structure of gum ghatti may be summarised in terms of the partial structures (I, II, and III), with the substituent groups R representing mainly single L-arabofuranose residues, but in a few cases more complex arabinose-containing side-chains terminated again by L-arabofuranose residues. Experiments to determine the mode of attachment of the aldobiouronic acid side-chains (II and III) to the backbone of galactose residues (I) will be reported later. It is already clear that gum ghatti resembles several other plant gums, notably damson, cherry, and egg-plum gums,[4-6] in containing a high proportion of L-arabofuranose residues in the outer parts of the molecular structure. It differs, however, from these gums in containing galactose residues mutually linked mainly through $C_{(1)}$ and $C_{(6)}$, and not through $C_{(3)}$ also. Gum

[3] For references see Aspinall and Schwarz, *Ann. Reports*, 1955, **52**, 267.
[4] Hirst and Jones, *J.*, 1938, 1174; 1939, 1482; 1946, 506.
[5] Jones, *J.*, 1939, 558; 1947, 1055; 1949, 3141.
[6] Hirst and Jones, *J.*, 1947, 1064; 1948, 120; 1949, 1757.

ghatti differs also in this respect from gum arabic, which is now known to contain a backbone of 1 : 3-linked D-galactopyranose units to which are attached side-chains of 1 : 6-linked galactose units.[7]

Experimental

Paper chromatography was carried out on Whatman No. 1 filter paper using the following solvent systems (v/v): (A) butan-1-ol–benzene–pyridine–water (5 : 1 : 3 : 3, upper layer); (B) ethyl acetate–acetic acid–water (3 : 1 : 3, upper layer); (C) butan-1-ol–acetic acid–water (4 : 1 : 5, upper layer); (D) butan-1-ol–ethanol–water (4 : 1 : 5, upper layer); (E) benzene–ethanol–water (169 : 47 : 15, upper layer); (F) ethyl acetate–acetic acid–formic acid–water (18 : 3 : 1 : 4); (G) butan-2-one, half saturated with water containing 1% of ammonia. Unless otherwise stated, chromatography of methylated sugars was carried out in solvent D and R_G values refer to rate of movement relative to 2 : 3 : 4 : 6-tetra-*O*-methyl-D-glucose in that solvent. Demethylations of methylated sugars were carried out by the procedure of Hough, Jones, and Wadman.[8] Paper ionophoresis was carried out in borate buffer at pH 10 at a potential of 500 v. Aniline derivatives of methylated sugars were prepared by refluxing the sugar in ethanolic aniline for 30 min.; further heating resulting in darkening of the solution. Optical rotations were observed at 18° ± 2°.

Samples of the gum acid and the degraded gum acid were prepared as described in Part I. During the preparation of the degraded gum acid the autohydrolysis of the gum acid caused the release of arabinose and only traces of xylose, rhamnose, and galactose. The various samples of degraded gum acid had slightly different optical rotations, $[\alpha]_D$ (as barium salt) varying from +2° to +9°. These samples were combined for subsequent experiments since the chromatographic patterns, after hydrolysis with N-sulphuric acid for 6 hr. at 100°, were similar in each case showing galactose in quantity, two aldobiouronic acids, small amounts of arabinose and mannose, and a trace of xylose.

Preparation and Hydrolysis of Methylated Degraded Gum.—The degraded gum (15 g.) was methylated extensively with methyl sulphate and sodium hydroxide following the procedure of Brown, Hirst, and Jones.[9] The product isolated as methylated degraded gum acid (8·2 g.; OMe, 36·9%) was further methylated with methyl iodide and silver oxide, giving methylated degraded gum (6·7 g.). Fractional precipitation of the methylated polysaccharide from chloroform by light petroleum gave fraction (*a*) (3·7 g.; OMe, 44·4%), which had $[\alpha]_D$ −28° (*c* 1·0 in $CHCl_3$), and fraction (*b*) (3·0 g.; OMe, 45·1%), which had $[\alpha]_D$ −11·5° (*c* 1·0 in $CHCl_3$). Chromatographic examination of the hydrolysates of the two fractions in solvent D showed similar complex mixtures of sugars.

Methylated degraded gum (fraction *a*; 3·2 g.) was suspended in N-hydrochloric acid (500 ml.) at 35° for 7 days, and the resulting solution was heated at 100° for 12·5 hr. (constant rotation), cooled, neutralised with silver carbonate, and filtered, and the filtrate was treated with hydrogen sulphide to remove silver ions, filtered, and concentrated. The resulting syrup was dissolved in water, and the solution was neutralised with barium carbonate, filtered, and concentrated to a dark syrup (3·0 g.). The dry syrup was repeatedly extracted with dry ether, to give an ether-soluble fraction (1·92 g.) and an ether-insoluble residue.

Examination of the Ether-soluble Fraction.—The syrup was separated on cellulose (60 × 3·4 cm.) with light petroleum (b. p. 100—120°)–butan-1-ol (7 : 3; later 1 : 1) saturated with water, and butan-1-ol partly saturated with water, as eluants, to give eight fractions, and a further fraction was obtained by elution of the cellulose with water.

Fraction 1. The syrup (23 mg.) contained a mixture of sugars (R_G 0·97—0·93) and a trace of tri-*O*-methylgalactose (R_G 0·72). Chromatographic examination in solvent E showed 2 : 3 : 4-tri-*O*-methylxylose and two sugars having similar mobilities and staining properties with aniline oxalate to 2 : 3 : 4-tri-*O*-methylrhamnose and 2 : 3 : 5-tri-*O*-methylarabinose. Demethylation gave galactose and traces of xylose and arabinose. The remainder of the syrup was hydrolysed with N-hydrochloric acid at 100 for 6 hr., and chromatography showed much di-*O*-methylgalactose in the hydrolysate. The origin of the latter sugar is obscure.

Fraction 2. The syrup (97 mg.) had $[\alpha]_D$ +100° (*c* 0·34) and R_G 0·89. The sugar was

[7] Dillon, O'Ceallachain, and O'Colla, *Proc. Roy. Irish Acad.*, 1953, **55**, *B*, 331; 1954, **57**, *B*, 31; Smith and Spriestersbach, Amer. Chem. Soc. Meeting, Minneapolis, Sept., 1955, Abs. Papers, 15D.
[8] Hough, Jones, and Wadman, *J.*, 1950, 1705.
[9] Brown, Hirst, and Jones, 1949, 1761.

identified as 2 : 3 : 4 : 6-tetra-*O*-methyl-D-galactose by conversion into the aniline derivative, m. p. and mixed m. p. 189—190°.

Fraction 3. Chromatography of the syrup (92 mg.) showed three components corresponding to 2 : 3 : 4 : 6-tetra-*O*-methylgalactose, 3 : 4 : 6-tri-*O*-methylmannose, and 2 : 3 : 4-tri-*O*-methylgalactose, R_G 0·89, 0·82, and 0·72. Demethylation gave galactose and mannose. Paper ionophoresis showed a component having the same mobility as 3 : 4 : 6-tri-*O*-methyl-D-mannose. Chromatographic examination of the products of periodate oxidation [2] showed 2 : 3 : 5-tri-*O*-methylarabinose (R_G 0·95) in addition to unchanged starting material. The syrup (50 mg.) was converted into the corresponding mixture of aldonamides, which, after treatment with sodium hypochlorite and addition of semicarbazide, afforded hydrazodicarbonamide, m. p. 268° and mixed m. p. (with sample of m. p. 263—264°) 264°.

Fraction 4. The chromatographically pure syrup (0·904 g.) had $[\alpha]_D$ +118° (*c* 0·42) and R_G 0·72 (Found: OMe, 41·7. Calc. for $C_9H_{18}O_6$: OMe, 41·8%). Demethylation gave only galactose. The sugar was identified as 2 : 3 : 4-tri-*O*-methyl-D-galactose by conversion into the aniline derivative, m. p. 165—167° and mixed m. p. (with sample of m. p. 159—161°) 159—162°. The sugar subsequently crystallised from acetone–ether as the monohydrate, m. p. 71° and mixed m. p. (with sample m. p. 73—76°) 72—73°.

Fraction 5. The syrup (112 mg.) contained two components, R_G 0·72 (2 : 3 : 4-tri-*O*-methylgalactose) and 0·60. The second component showed similar chromatographic and ionophoretic behaviour to 3 : 4-di-*O*-methyl-D-mannose. The mixture gave galactose and mannose on demethylation. Attempts to separate the two components by chromatography on Amberlite resin IRA-400 (borate form) were unsuccessful.

Fraction 6. The syrup (203 mg.) contained two components, having R_G 0·49 and 0·75 respectively, the coloration of the former with aniline oxalate suggesting 2 : 3-di-*O*-methylgalactose. Demethylation gave only galactose. Separation of the syrup (190 mg.) on filter sheets using solvent D gave fractions 6*a* (70 mg.) and 6*b* (54 mg.). Paper ionophoresis of fraction 6*a* showed 2 : 3-di-*O*-methylgalactose and a trace of the 2 : 4-dimethyl ether. Chromatographic examination of the products of periodate oxidation [2] confirmed the presence of 2 : 3-di-*O*-methylgalactose. An authentic sample of 2 : 3-di-*O*-methyl-D-galactose when oxidised with periodate showed three oxidation products with R_F 0·66 (grey), 0·78 (brown), and 0·87 (grey) respectively, whereas 2 : 4-di-*O*-methyl-D-galactose showed only unchanged sugar (R_F 0·37). The sugar had $[\alpha]_D$ +69° ⟶ +80° (*c* 0·37) and the identity of the main component was proved by conversion into 2 : 3-di-*O*-methyl-*N*-phenyl-D-galactosylamine, m. p. 125—128° and mixed m. p. 124—127°. Fraction 6*b* was hydrolysed with N-hydrochloric acid for 6 hr. at 100° and chromatographic examination showed only 2 : 3 : 4-tri-*O*-methylgalactose; it is probable that this fraction contains a polymer of 2 : 3 : 4-tri-*O*-methyl-D-galactose arising from incomplete hydrolysis of the methylated polysaccharide.

Fraction 7. The syrup (91 mg.) contained at least two components (having R_G 0·48 and 0·75 respectively). Separation of the mixture (88 mg.) on filter sheets using solvent D gave fractions 7*a* (53 mg.) and 7*b* (17 mg.). Paper ionophoresis and chromatographic examination of the products of periodate oxidation [2] indicated the presence in fraction 7*a* of 2 : 3- and 2 : 4-di-*O*-methylgalactose. The presence in the mixture of 2 : 4-di-*O*-methyl-D-galactose was shown by conversion into the aniline derivative, m. p. and mixed m. p. 202—204°. Fraction 7*b* contained the same substance (R_G 0·75) as fraction 6*b* and small amounts of di-*O*-methylgalactose. On hydrolysis the main component gave 2 : 3 : 4-tri-*O*-methylgalactose.

Fraction 8. The syrup (31 mg.) contained a di-*O*-methylgalactose (R_G 0·45) and small amounts of 4-*O*-methylmannose and an unidentified sugar (R_G 0·65).

Fraction 9. The syrup (48 mg.) contained a complex mixture of acidic and neutral sugars and was not examined further.

Examination of the Ether-insoluble Fraction.—The ether-insoluble residue was treated with Amberlite resin IR-120(H) to remove barium ions, and concentration gave a syrup (0·714 g.) (equiv. wt., 597). Chromatography showed neutral sugars in addition to acidic substances. The syrup (0·63 g.) was dissolved in water and neutralised with barium carbonate, and the resulting mixture was separated on filter sheets using solvent D, to give barium salts (A) (365 mg.), and fractions B (i) (190 mg.) and B (ii) (92 mg.), both contaminated with acidic substances. Chromatography showed fraction B (i) to contain mainly 2 : 3 : 4-tri-*O*-methylgalactose (R_G 0·72), and fraction B (ii) to contain di-*O*-methylgalactose (ionophoresis and chromatography of the periodate oxidation products [2] indicating the 2 : 3-isomer to be the

main component). A sample (25 mg.) of barium salts (A) was treated with Amberlite resin IR-120(H) to give a mixture of acids (equiv. wt., 370, indicating mainly aldobiouronic acid) which on hydrolysis yielded acidic and neutral sugars.

Barium salts (A) (330 mg.) were converted into the corresponding acids (307 mg.) which were hydrolysed with N-hydrochloric acid at 100° for 7 hr. After neutralisation with silver carbonate, separation on filter sheets in solvent D afforded neutral sugars [fractions C (i)—C (iv)] and silver salts (D). The silver salts (D) were converted into acids (143 mg.) which were separated on filter sheets by solvent C into fractions D (i) (48 mg.) and (D) (ii) (36 mg.).

Fraction C (i) (9 mg.) contained 3 : 4 : 6-tri-*O*-methylmannose (R_G 0·82). Fraction C (ii) (35 mg.) contained 2 : 3 : 4-tri-*O*-methyl-D-galactose (R_G 0·72), identified as the aniline derivative, m. p. 159—162° and mixed m. p. 156—159°. Fraction C (iii) (26 mg.) contained 2 : 3 : 4-tri-*O*-methylgalactose (R_G 0·72) and a trace of a second component (R_G 0·60). Fraction C (iv) (28 mg.) contained di-*O*-methylgalactose (R_G 0·49), shown by ionophoresis and chromatography of the periodate oxidation products [2] to be mainly the 2 : 3-dimethyl ether. Fraction (i) was chromatographically pure 2 : 3 : 4-tri-*O*-methylglucuronic acid. Attempts to characterise the sugar by conversion into the crystalline amide of methyl 2 : 3 : 4-tri-*O*-methyl-α-D-glucuronoside failed. The syrupy product was treated with methanolic hydrogen chloride, and the resulting ester was reduced with lithium aluminium hydride and hydrolysed. Chromatography showed only 2 : 3 : 4-tri-*O*-methylglucose (R_G 0·85). Fraction D (ii), which contained at least three components, was converted into the methyl ester methyl glycosides, reduced with lithium aluminium hydride, and hydrolysed. Chromatography showed 2 : 3-di-*O*-methylglucose, small amounts of tri- and di-*O*-methylgalactose, and a trace of 2 : 3 : 4-tri-*O*-methylglucose.

Preparation and Hydrolysis of Methylated Gum.—The gum acid (25 g.) was methylated extensively with methyl sulphate and sodium hydroxide by the procedure of Brown, Hirst, and Jones.[9] The product isolated as the methylated gum acid (18 g.; OMe, 35·0%; ash, 5·8%) was further methylated with methyl iodide and silver oxide (three treatments) to give methylated gum (7·3 g.), $[\alpha]_D$ −72° (*c* 1·0 in $CHCl_3$) (Found: OMe, 42·8%).

The methylated gum (7·3 g.) was refluxed with methanolic 2% hydrogen chloride (500 ml.) for 12 hr. (constant rotation). Methanol was removed under reduced pressure and the product was heated with 0·55N-hydrochloric acid (600 ml.) on the boiling-water bath for 12 hr. (constant rotation). The cooled solution was neutralised with silver carbonate, then filtered, and hydrogen sulphide was passed through the filtrate to precipitate silver ions, and the filtrate was concentrated. Sugars were extracted from the residue with methanol, and the resulting syrup was dissolved in water, neutralised with barium carbonate, filtered, and concentrated to a syrup (7·3 g.).

The mixture of methylated sugars (7·3 g.) was repeatedly extracted with dry ether to give ether-soluble sugars (A) (4·76 g.) and an ether-insoluble residue (B) (2·10 g.). The ether-insoluble sugars (B) were separated into neutral and acid fractions by chromatography on cellulose (50 × 2·5 cm.) with butan-1-ol, 80% saturated with water, as eluant, four fractions being isolated. Fraction (C) (0·80 g.) contained a mixture of neutral sugars. Fraction (D) (0·224 g.) contained chromatographically pure 2-*O*-methyl-D-galactose, m. p. 157—158° (from acetone–water), $[\alpha]_D$ +55° (5 min.) ⟶ +89° (120 min., const.) (*c* 1·91 in H_2O). Fraction (E) (0·14 g.) contained a mixture of 2-*O*-methylgalactose and acidic sugars. Fraction (F) (0·398 g.) contained acidic components and a trace of 2-*O*-methylgalactose.

Examination of Neutral Methylated Sugars.—The ether-soluble sugars (A) and fraction (C) were combined and separated on cellulose (76 × 3·5 cm.) with light petroleum (b. p. 100—120°)–butan-1-ol (7 : 3; later, 1 : 1) saturated with water, and butan-1-ol partly saturated with water as eluants, to give eighteen fractions. A further fraction (19) (64 mg.) was obtained by elution of the cellulose with water.

Fraction 1. The syrup (119 mg.) had $[\alpha]_D$ +15° (*c* 0·39), and chromatography showed a main component having R_G 1·03 (cf. 2 : 3 : 4-tri-*O*-methyl-L-rhamnose) and traces of other sugars. Chromatography in solvent E showed a second component travelling faster. Hydrolysis of a sample with N-sulphuric acid, followed by neutralisation with barium carbonate and chromatography showed tri-*O*-methylrhamnose, 2 : 3 : 5-tri-*O*-methylarabinose, and the barium salt of an acid (at the starting line of the paper). Treatment of a second sample with cold barium hydroxide, followed by neutralisation with carbon dioxide and chromatography, gave a similar result. The remaining syrup (*ca.* 80 mg.) was treated with cold 5% barium hydroxide solution for 30 min., and the solution was neutralised with carbon dioxide, filtered

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and concentrated. The product was separated on a filter sheet with solvent D, to give fractions **1***a* and **1***b*. Fraction **1***a* contained 2 : 3 : 4-tri-*O*-methylrhamnose (R_G 1·03) and a trace of 2 : 3 : 5-tri-*O*-methylarabinose (R_G 0·97). The main component was identified by conversion into 2 : 3 : 4-tri-*O*-methyl-*N*-phenyl-L-rhamnosylamine, m. p. and mixed m. p. 98—100°. Fraction **1***b* (barium salt) was deionised with Amberlite resin IR-120(H), and chromatography in solvent C showed 2 : 3 : 4-tri-*O*-methylglucuronic acid. Conversion of the acid into the methyl ester methyl glycoside with dry methanolic hydrogen chloride, followed by reduction with lithium aluminium hydride in methylal, hydrolysis with N-hydrochloric acid, and chromatography in solvent D, showed only 2 : 3 : 4-tri-*O*-methylglucose. It is concluded that tri-*O*-methylglucuronic acid was present in fraction **1** as an ester.

Fraction **2**. Chromatography of the syrup (150 mg.) showed 2 : 3 : 5-tri-*O*-methylarabinose and a trace of 2 : 3 : 4-tri-*O*-methylrhamnose. The optical rotation, $[\alpha]_D$ −41° (*c* 0·59), indicated almost pure 2 : 3 : 5-tri-*O*-methyl-L-arabinose (cf. 2 : 3 : 5-tri-*O*-methyl-L-arabinose,[10] $[\alpha]_D$ −39·5°).

Fraction **3**. The syrup (1·835 g.), which had $[\alpha]_D$ −42·5° (*c* 0·68), was almost pure 2 : 3 : 5-tri-*O*-methyl-L-arabinose with a trace of 2 : 3 : 4 : 6-tetra-*O*-methylgalactose. Demethylation gave arabinose and a trace of galactose. The identity of the main component was confirmed by conversion into 2 : 3 : 5-tri-*O*-methyl-L-arabonamide, m. p. 132—133° and mixed m. p. (with sample of m. p. 129—130°) 129°.

Fraction **4**. Chromatography of the syrup (34 mg.), which had $[\alpha]_D$ +66° (*c* 0·48), showed a single component, R_G 0·97. Re-examination in solvent E showed 2 : 3 : 4-tri-*O*-methylxylose, 2 : 3 : 5-tri-*O*-methylarabinose, and an unidentified sugar. Demethylation gave xylose, arabinose, and galactose.

Fraction **5**. Chromatography of the syrup (34 mg.) which had $[\alpha]_D$ +30° (*c* 0·59) in solvent E, showed 2 : 3 : 4 : 6-tetra-*O*-methylgalactose and 2 : 3 : 5-tri- and di-*O*-methylarabofuranose. The presence of 2 : 3 : 4 : 6-tetra-*O*-methyl-D-galactose was shown by conversion into the aniline derivative, m. p. and mixed m. p. 179—180°.

Fraction **6**. The syrup (17 mg.) had $[\alpha]_D$ −35° (*c* 0·29) and chromatography showed a main component with R_G 0·83, giving a brown stain (and yellow fluorescence in ultraviolet light) with aniline oxalate (cf. 3 : 5-di-*O*-methyl-L-arabinose, R_G 0·83). Demethylation gave arabinose and traces of galactose and mannose. Paper ionophoresis showed that 3 : 4 : 6-tri-*O*-methylmannose (R_G 0·82) and 2 : 5- (R_G 0·85) and 3 : 5-di-*O*-methylarabinose (R_G 0·83) could be readily distinguished in mixtures; fraction **6** showed mainly 3 : 5-di-*O*-methylarabinose with small amounts of the other two sugars.

Fraction **7**. The syrup (230 mg.), which had $[\alpha]_D$ −24° (*c* 0·42), was shown by chromatography and ionophoresis to contain approximately equal amounts of 2 : 5- and 3 : 5-di-*O*-methylarabinose. Attempts to separate the two components by gradient elution from charcoal containing borate buffer (pH 10) with butan-2-one [11] were unsuccessful. The major portion (160 mg.) was fractionated by elution from Amberlite resin IRA-400 (borate form) with 0·5M-boric acid.[12] Although much sugar was irreversibly absorbed on the resin, two ionophoretically pure fractions **7***a* (40 mg.) and **7***b* (10 mg.) were obtained. Fraction **7***a* was identified as 2 : 5-di-*O*-methyl-L-arabinose by conversion into 2 : 5-di-*O*-methyl-L-arabonamide, m. p. 122° and mixed m. p. 123—124°. Fraction **7***b* was identified as 3 : 5-di-*O*-methyl-L-arabinose by conversion into 3 : 5-di-*O*-methyl-L-arabonolactone, m. p. 65° and mixed m. p. (with sample m. p. 69—71°) 67—69°.

Fraction **8**. Chromatography and ionophoresis showed the syrup (80 mg.) to contain 2 : 5- and 3 : 5-di-*O*-methylarabinose, 3 : 4 : 6-tri-*O*-methylmannose, and a trace of 2 : 3 : 4-tri-*O*-methylgalactose. Attempts to separate the components by chromatography on charcoal containing borate buffer [11] failed.

Fraction **9**. The syrup (174 mg.), which had $[\alpha]_D$ +72° ⟶ +119° (*c* 0·42), contained two components, R_G 0·65 and 0·70 respectively, present in approximately equal quantities and indistinguishable from 2 : 3-di-*O*-methylarabinose and 2 : 3 : 4-tri-*O*-methylgalactose. Demethylation gave arabinose and galactose. The syrup was converted into the corresponding mixture of aldonamides, from which 2 : 3-di-*O*-methyl-L-arabonamide readily crystallised, m. p. 154° and mixed m. p. 153—154°.

[10] Baker and Haworth, *J.*, 1925, 365.
[11] Bouveng and Lindberg, *Acta Chem. Scand.*, 1956, **10**, 1283.
[12] Lock and Richards, *J.*, 1955, 3025.

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Fraction 10. The chromatographically pure syrup (299 mg.) had $[\alpha]_D$ +109° (*c* 0·51) and R_G 0·70. Recrystallisation from acetone–ether afforded 2 : 3 : 4-tri-*O*-methyl-D-galactose hydrate, m. p. 66—67°. The derived 2 : 3 : 4-tri-*O*-methyl-*N*-phenyl-D-galactosylamine had m. p. and mixed m. p. 161—162°.

Fraction 11. Chromatography of the syrup (59 mg.), which had $[\alpha]_D$ +88° (*c* 0·33), showed 2 : 3 : 4-tri-*O*-methylgalactose (R_G 0·70) and a trace of an unknown sugar (R_G 0·52). The main component was identified by conversion into 2 : 3 : 4-tri-*O*-methyl-*N*-phenyl-D-galactosylamine, m. p. and mixed m. p. 164—165°.

Fraction 12. Chromatography of the syrup (155 mg.) showed a main component, R_G 0·60, and a small amount of 2 : 3 : 4-tri-*O*-methylgalactose. Demethylation gave arabinose and a small amount of galactose. The optical rotation, $[\alpha]_D$ +118° (*c* 0·38), indicated that the major component was a di-*O*-methyl-L-arabopyranose. Chromatographic examination in solvent F differentiated the sugar from 2 : 3- and 3 : 4-di-*O*-methylarabinose, and ionophoresis showed 3 : 4-di-*O*-methylarabinose to be absent. The syrup (60 mg.), when heated with ethanolic aniline, afforded an aniline derivative, m. p. 129—130° and mixed m. p. (with sample, 139—140°) 125—126°, whose *X*-ray powder photograph was identical with that of 2 : 4-di-*O*-methyl-*N*-phenyl-L-arabinosylamine.

Fraction 13. Chromatography of the syrup (280 mg.), which had $[\alpha]_D$ +55° (*c* 0·29), showed a major component (R_G 0·49), a small amount of tri-*O*-methylgalactose, and a trace of a sugar (R_G 0·32) suspected of being 2-*O*-methylarabinose. Demethylation gave galactose and a trace of arabinose. Paper ionophoresis showed three components, a small component travelling at the same rate as 2 : 3-di-*O*-methylgalactose, an unidentified component in traces [(?) 2-*O*-methylarabinose], and the main component stationary (cf. 2 : 4-di-*O*-methylgalactose). Chromatography of the products of periodate oxidation showed 2 : 4-di-*O*-methylgalactose (R_F 0·37, unchanged), and small amounts of oxidation products with R_F 0·66 (grey), 0·78 (brown), and 0·15 (bright yellow). The first two oxidation products are formed from 2 : 3-di-*O*-methylgalactose, and the third from 2-*O*-methylaldoses (probably from 2-*O*-methylarabinose). The major component was identified as 2 : 4-di-*O*-methyl-D-galactose by conversion into the aniline derivative, m. p. and mixed m. p. 206—208°.

Fraction 14. The chromatographically pure sugar (393 mg.) crystallised from acetone–water and had m. p. and mixed m. p. (with 2 : 4-di-*O*-methyl-D-galactose monohydrate) 97—99° and $[\alpha]_D$ +133° ⟶ +89° (equil.) (*c* 0·54) (Found: OMe, 27·8. Calc. for $C_8H_{16}O_6,H_2O$: OMe, 27·4%). The derived 2 : 4-di-*O*-methyl-*N*-phenyl-D-galactosylamine had m. p. and mixed m. p. 213—214°.

Fraction 15. Chromatography of the syrup (109 mg.) showed 2 : 4-di-*O*-methylgalactose, a sugar with R_G 0·36, and a trace of (?) 2-*O*-methylarabinose. Demethylation gave galactose, mannose, and a trace of arabinose. Ionophoresis showed di-*O*-methylgalactose (stationary), and a second sugar moving faster than 2- and 3-*O*-methylmannose. Separation of the syrup (100 mg.) on cellulose with solvent G gave fractions 15*a* and 15*b*. Fraction 15*a* contained 2 : 4-di-*O*-methylgalactose and (?) 2-*O*-methylarabinose (R_G 0·32) and gave galactose and arabinose on demethylation. Chromatography of the products of periodate oxidation [2] showed unchanged di-*O*-methylgalactose and a component, R_F 0·15 (bright yellow), formed from 2-*O*-methylaldoses. Fraction 15*b* was identified as 4-*O*-methyl-D-mannose by conversion into 4-*O*-methyl-D-mannonolactone, m. p. and mixed m. p. 159—160°.

Fraction 16. Chromatography of the syrup (47 mg.) showed 4-*O*-methylmannose (R_G 0·36) and a second sugar in smaller amount (R_G 0·32). The optical rotation, $[\alpha]_D$ +43° ⟶ +37° (*c* 0·33) (cf. 4-*O*-methyl-D-mannose, $[\alpha]_D$ +32° ⟶ +22°), and methoxyl content (Found: OMe, 17·3. Calc. for $C_7H_{14}O_6$: OMe, 16·0. Calc. for $C_8H_{12}O_5$: OMe, 18·9%) were consistent with those of a mixture of 4-*O*-methyl-D-mannose and a mono-*O*-methyl-L-arabinose. Furthermore, chromatography showed periodate oxidation products with R_F 0·60 (brown) and 0·15 (yellow) identical with those from 4-*O*-methyl-D-mannose and 2-*O*-methylaldoses. Attempts to characterise the sugar by conversion into 4-*O*-methyl-D-glucosazone failed, although an impure fraction, m. p. 135—136°, was shown by circular paper chromatography to contain the desired compound together with a second component.

Fraction 17. Chromatography showed the syrup (84 mg.) to contain 2 : 4-di-*O*-methylgalactose, 4-*O*-methylmannose, and 2-*O*-methylgalactose.

Fraction 18. The chromatographically pure sugar (431 mg.; R_G 0·25) crystallised from glacial acetic acid and had m. p. and mixed m. p. (with 2-*O*-methyl-D-galactose) 146—147°

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and $[\alpha]_D$ +64° ⟶ +91° (equil.) (*c* 0·37). After recrystallisation from acetone–water the sugar had m. p. 154°.

Examination of Acidic Components.—Acidic fractions (F) and (19) (as barium salts), containing a trace of 2-*O*-methylgalactose, were combined and dissolved in water, barium ions were removed by passage through Amberlite resin IR-120(H), and the solution was concentrated to a syrup (376 mg.). The mixture of acids was refluxed with methanolic 1·3% hydrogen chloride (50 ml.) for 6 hr. The product, after neutralisation with silver carbonate and concentration, was dissolved in formaldehyde dimethyl acetal (40 ml.), lithium aluminium hydride (0·2 g.) was added, and the solution was refluxed for 2 hr. Excess of hydride was destroyed by water, the acetal layer was separated, the aqueous layer was taken to dryness, and the residue was extracted with chloroform and acetone. The combined organic extracts were concentrated to a syrup (330 mg.) which was hydrolysed with N-hydrochloric acid (30 ml.) for 6 hr. at 100° to give, after neutralisation and concentration, a syrupy mixture of sugars (230 mg.). Separation of the methylated sugars on cellulose (50 × 2·5 cm.) with light petroleum (b. p. 100—120°)–butan-1-ol (1 : 1), saturated with water, as eluant, gave nine fractions. Fraction *a* (21 mg., R_G 0·85) was identified as 2 : 3 : 4-tri-*O*-methyl-D-glucose by conversion into the aniline derivative, m. p. and mixed m. p. 134—135°. Fraction *b* (19 mg.; R_G 0·72 and 0·58) contained 2 : 3 : 4-tri-*O*-methylgalactose and 2 : 3-di-*O*-methylglucose (major component). Fraction *c* (47 mg.; R_G 0·58) was identified as 2 : 3-di-*O*-methyl-D-glucose by chromatography of the sugar and its periodate oxidation products [R_F 0·73 (bright yellow) and 0·63 (brown), ionophoresis, and by conversion into 2 : 3-di-*O*-methyl-D-gluconophenylhydrazide, m. p. 173—174° and mixed m. p. (with sample, m. p. 168—169°) 169—171°. Fraction *d* (11 mg.; R_G 0·58 and 0·54) contained 2 : 3-di-*O*-methylglucose and a trace of an unidentified sugar. Fraction *e* (9 mg.; R_G 0·49) was identified as 2 : 4-di-*O*-methyl-D-galactose by conversion into the aniline derivative, m. p. and mixed m. p. 212—214°. Fraction *f* (10 mg.; R_G 0·49 and 0·36) contained a mixture of 2 : 4-di-*O*-methylgalactose and 4-*O*-methylmannose. Fraction *g* (20 mg.; R_G 0·36) was identified as 4-*O*-methyl-D-mannose by chromatography of the sugar and its periodate oxidation product [R_F 0·60 (brown)], ionophoresis, and by conversion into 4-*O*-methyl-D-mannonolactone, m. p. and mixed m. p. (with sample of m. p. 161—162°) 150—151°. Fraction *h* (13 mg.; R_G 0·32) contained at least two components giving periodate oxidation products having R_F 0·60 (brown) and 0·15 (bright yellow). Fraction *j* (8 mg.; R_G 0·25) was identified as 2-*O*-methyl-D-galactose by chromatography of the sugar and its periodate oxidation product R_F 0·23 (bright yellow), and as the crystalline sugar, m. p. and mixed m. p. 139—140°.

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48. *Adsorption of Gold from Cyanide Solutions by Anionic Resins.*

By J. Aveston, D. A. Everest, and R. A. Wells.

Adsorption of anions on both strong- and weak-base ion-exchange resins is a function of the charge on the anion, its polarisability as measured by ionic refractivity and, less, of its shape and chemical nature. The swollen volume of a resin in a given salt form depends upon similar factors. The high affinity of Amberlite I.R.A. 400 for complex cyanides in general is due to their high polarisability. With multivalent anions adsorption is limited by the increased distance between the ionised resin sites and the equilibrium position of the adsorbed anion at the " centre of gravity " of these groups which reduces the polarisation of these anions by the resin cation groups. This effect becomes most important with weak-base resins in alkaline solution, the distance between the resin sites and the multivalent anions becoming large relative to the ionic radii of the latter owing to the low degree of ionisation of the resin. The multivalent anions are then displaced by highly polarisable singly charged ions, such as aurocyanide, as singly charged ions can take up the same position relative to the ionised resin sites irrespective of the spacing of the functional groups in the resin matrix. It has been calculated that the selectivity coefficients for aurocyanide's displacing a multivalent anion should decrease logarithmically with the four-third root of the capacity on a volume basis if the cross-linking of the resin remains constant; this relation holds in practice.

Gold, as aurocyanide ion, is strongly adsorbed [1] by the strong-base resin Amberlite I.R.A. 400 from alkaline cyanide solutions. Base-metal complex cyanides are also strongly adsorbed by this resin and, as these predominate in actual cyanide liquors, they must be selectively eluted before the gold if the resin is to be used for gold recovery. Aurocyanide can be selectively adsorbed [2] (by weak-base resins) from cyanide liquors containing excess of base-metal cyanides, thus making such preliminary elution unnecessary. Complete elution of the gold was somewhat difficult from both strong- and weak-base resins, but was satisfactory when organic solvent–mineral acid mixtures or aqueous solutions containing thiocyanate or perchlorate ions were used. The introduction of *ca.* 8—10% of strong-base groups, out of the total active groups present, increased the weight of gold adsorbed from a given solution by a weak-base resin, although this was at the expense of some selectivity of the resin for gold.

We have tried to interpret these results theoretically and, in particular, to explain the much greater selectivity of weak-base resins for aurocyanide over the base-metal cyanides than that of strong-base resins. We have tried to generalise the results for application to all anion-exchange systems.

Experimental

Equilibria with Amberlite I.R.A. 400 (40/60 mesh, capacity 3·74 mequiv./g. of dry chloride form) were measured by using ^{198}Au as tracer, this being prepared by neutron bombardment of ^{197}AuCN in the Harwell pile, followed by dissolution of the product in the calculated quantity of potassium cyanide solution. The resulting solution had pH 7 and contained no excess of cyanide ions. Solutions containing potassium aurocyanide of known specific activity, together with a known concentration of the sodium salt of the exchangeable ion A^- being studied, and sufficient resin in the A^- form to adsorb a large proportion of the aurocyanide, were contained in a 250 ml. beaker fitted with a magnetic stirrer and the solution was circulated continuously through a flow counter tube connected to a count ratemeter and pen recorder by means of a " Sigma " pump. Resin was kept out of the counter tube by a sintered-glass disc on the end of

[1] Burstall, Forrest, Kember, and Wells, *Ind. Eng. Chem.*, 1953, **45**, 1648.
[2] Aveston, Everest, Kember, and Wells, *J. Appl. Chem.*, 1957, in the press.

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the pump intake tube. The natural activity of the potassium associated with the aurocyanide was always an insignificant fraction of the total activity. From the activity of the solution at resin–solution equilibrium (after 1—2 hr.) and the activity of the original aurocyanide solution added (after application of decay and dead-time and background corrections), the amount of gold in solution at equilibrium, and hence the amount of gold adsorbed by the resin and the amount of A^- liberated from the resin, were calculated. Sufficient data were thus available to calculate K_A^{Au} (the equilibrium constant for aurocyanide displacing the ion A^- from the resin) at that particular gold loading. Repetition of this procedure by addition of further aliquot portions of aurocyanide to the same solution gave further values of K_A^{Au} at higher gold loadings. A complete curve of K_A^{Au} at various gold loadings on the resin was thus obtained.

The pure weak-base resin J.A.1 was prepared from chloromethylated polystyrene containing $3\frac{1}{2}\%$ of divinylbenzene by treatment with anhydrous dimethylamine in dry dioxan. The few strong-base groups in the product were eliminated by heating the free-base form at 100° under vacuum for 2 hr.[3] The resin had a capacity of 4·10 mequiv./g. of dry chloride form.

The low-capacity strong-base resins were prepared from polystyrene beads containing either 2% or 8% of divinylbenzene. The beads were first allowed to swell in ten times their weight of chloromethyl ether (b. p. 58—59°) for 24 hr. at 4°, stannic chloride catalyst (0·1%) was added, and the beads left for a further 24 hr. at 4°. The mixture was then heated to 50° for periods of between 15 min. and 48 hr., depending upon the final capacity desired. The chloromethylated polystyrene beads were washed with dioxan and aminated by treating them with 25% aqueous trimethylamine at 20° for two days.

Results and Discussion

Experiments with Amberlite I.R.A. 400.—Application of the law of mass action to the displacement of A^{z-} from an ion-exchange resin by a univalent anion B^-, *i.e.*, to the equilibrium

$$A^{z-}(r) + zB^-(s) \rightleftharpoons zB^-(r) + A^{z-}(s)$$

where (r) refers to the resin and (s) to the solution phase, leads directly to the expression

$$\frac{[B^-(r)]^z[A^{z-}(s)]}{[B^-(s)]^z[A^{z-}(r)]} \cdot \frac{\gamma A^{z-}(s)}{(\gamma B^-(s))^z} = Kd \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where the terms in [square] brackets refer to molalities in either phase and the γ's are ion activity coefficients. Kd is the practical molal selectivity coefficient determined experimentally. In all experiments now described the solutions were very dilute and the solution activity coefficients are taken as unity.

The values of Kd for aurocyanide displacing a number of different ions from the resin (*i.e.*, K_A^{Au}, see above), determined at different gold loadings, are plotted in Fig. 1 against the mole fraction of the resin in the aurocyanide form (X_{Au}). The mean values of Kd (*i.e.*, $K'd$, when $K'd = \int_0^{'} Kd \,.\, dX_{Au}$) are given in Table 1. No detailed attempt was made to explain the shape of the Kd curves in Fig. 1 although more regular behaviour is

Table 1. *Selectivity coefficients of various anions against aurocyanide on Amberlite I.R.A. 400.*

Type of ion	Ion = A	$K'_A{}^{Au}$	log $K'_A{}^{Au}$	Type of ion	Ion = A	$K'_A{}^{Au}$	log $K'_A{}^{Au}$
Spherical	F^-	5500	3·74	Pyramidal	ClO_3^-	50 *	1·70
	Cl^-	692	2·84		BrO_3^-	195 *	2·29
	Br^-	165	2·22		IO_3^-	250 *	2·40
	I^-	36	1·56				
				Square-planar	$[Ni(CN)_4]^{2-}$	246	2·39
Linear	CNS^-	9·6	0·98		$[Pd(CN)_4]^{2-}$	76	1·88
	$[Ag(CN)_2]^-$	5·75	0·76		$[Pt(CN)_4]^{2-}$	49·6	1·695
	$[Au(CN)_2]^-$	1·0	0·00				
				Octahedral	$[Co(CN)_6]^{3-}$	$8·0 \times 10^9$	9·90
Tetrahedral	BF_4^-	26	1·415		$[Fe(CN)_6]^{3-}$	$6·0 \times 10^9$	9·78
	ClO_4^-	4·6	0·66				
	MnO_4^-	0·53	−0·28				
	ReO_4^-	3·8	0·58				

* $K'd$ obtained from $\int_0^{0.5} Kd \,.\, dX_{Au}$

obtained if the exchange takes place between ions of similar type, *e.g.*, linear ions such as $[Au(CN)_2]^-$ and CNS^- where the ratio $\gamma[Au(CN)_2]^-/\gamma CNS^-$ in the resin phase should be approximately constant. The variations found in *Kd* with resin loading may be due to a change in ionic strength in the resin phase as the composition varies between a largely ionic form (*e.g.*, chloride) where the polarisation forces are small and one where the polarisation forces are large, resulting in a high degree of association between the resin sites and the adsorbed ion. The significance of polarisation forces in anionic resin systems is discussed below.

FIG. 1

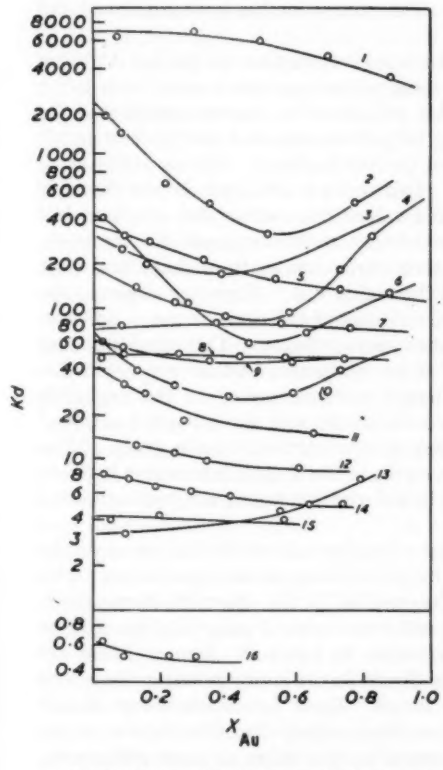
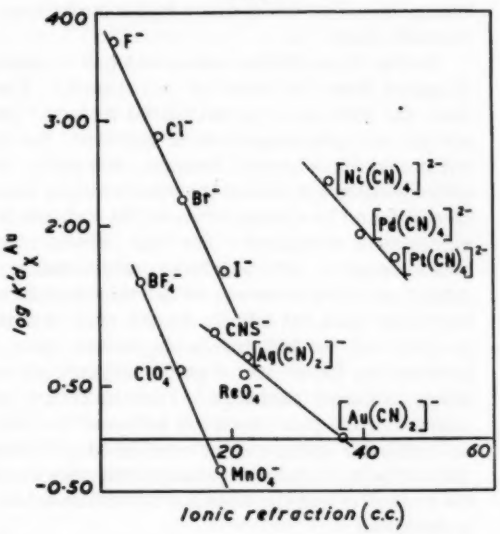


FIG. 2.



1 F^-, 2 Cl^-, 3 $[Ni(CN)_4]^{2-}$, 4 IO_3^-, 5 BrO_3^-, 6 Br^-, 7 $[Pd(CN)_4]^{2-}$, 8 ClO_3^-, 9 $[Pt(CN)_4]^{2-}$, 10 I^-, 11 BF_4^-, 12 CNS^-, 13 ReO_4^-, 14 $[Ag(CN)_2]^-$, 15 ClO_4^-, 16 MnO_4^-.

Most of the selectivity coefficients measured are far from unity and usually vary largely with resin composition.

With a cation-exchange resin Kressman and Kitchener [3] found that the observed equilibria are represented quite well by the law of mass action if concentration is used in place of activities in the resin phase. Moreover, the equilibrium constants for the exchange between ammonium ions and the alkali metals are a function of the hydrated ionic size of the exchanging ions expressed as the a° parameter of the Debye–Hückel theory. This leads to preferential adsorption of the ion with the smaller hydrated radius. Apparent exceptions to this relationship, such as occurred with the thallous ion, are explained on the basis of the incomplete dissociation in solution of the salts of the cation concerned. This factor should not normally be important here owing to the exclusive use of the sodium and potassium salts of the anions.

In general it can be considered that there are three main factors operating between a

[3] Kressman and Kitchener, *J.*, 1949, 1190.

resin functional group and an adsorbed ion: (*a*) coulombic forces, (*b*) polarisation forces, and (*c*) van der Waals forces and ion–dipole interactions. The polarisabilities of cations are usually small, so that with all but the largest cations the coulombic forces are chiefly responsible for the binding of cations to a resin, as has been often confirmed.[3-7] However, Gregor *et al.*[8] showed that the selectivity coefficients obtained on Dowex 2 for the exchange of a given anion with the halide ions is a linear function of the polarisability of the latter as measured by their ionic refractions, their affinity for the resin increasing with increase in their polarisability, *i.e.*, from fluoride to iodide. This suggests that anion-exchange systems are not governed only by coulombic forces as are cation-exchange systems, but that polarisation forces are of major importance. This conclusion has been confirmed and extended here.

In Fig. 2 are plotted values of log $K'd$ against the ionic refraction for the ion A^- being displaced from the resin by aurocyanide. The ionic refraction values have been taken from the literature [9] or calculated from the molar refraction in aqueous solution of the sodium and potassium salts of the ions. Except for per-rhenate and the three trigonal-pyramidal ions chlorate, bromate, and iodate (not plotted in Fig. 2) all ions of the same geometrical shape fall on the same straight line. This result is obtained despite the wide spread found in certain cases in the individual Kd values from which the averaged $K'd$ values were calculated. The high affinity of perchlorate and thiocyanate for the resin, which Gregor *et al.*[8] considered exceptional, are thus explicable by their shape and ionic refraction in the same way as are the affinities of the halide ions. The steep slopes of the lines show that the affinity for the resin of a series of ions of the same shape is not only proportional to, but highly dependent upon, their polarisability. This confirms that polarisation forces are of prime importance in anion exchange, just as are coulombic forces in cation exchange. Thus in cation-exchange systems, owing to the negligible amount of ion-pair formation between the ionised resin sites and the adsorbed cations,[7] no particular cation can be considered as belonging to any particular resin group. This will not be true of anion-exchange processes where, owing to the greater interaction between the resin sites and the adsorbed anions caused by the polarisation forces, ion-pair formation is favoured.

That perrhenate does not fall on the same ionic refraction–selectivity curves as do the other univalent tetrahedral ions (Fig. 2) may be due to its being present in solution partly as the meso-form ReO_5^{3-}. With chlorate, bromate, and iodate the observed discrepancies may be due partly to the fact that the principal and lesser axes of polarisability of these ions appear to become more nearly equal from chlorate to iodate.[10] Also, as these are the only unsymmetrical ions studied here, the ion–dipole forces acting between these ions and the resin sites may oppose the polarisation forces. These ion–dipole forces should decrease from chlorate to iodate owing to the greater electronegativity of the chlorine atom. These two effects reverse the affinity order expected on the basis of ionic refractions, making it $ClO_3^- > BrO_3^- > IO_3^-$.

Thus the greater the degree of interaction between an adsorbed anion and the charged resin sites, *i.e.*, the greater the polarisation forces, the greater the affinity of that anion for the resin. The relatively low selectivity of the resin for the highly polarisable bivalent ions nickel(II) and platinum(II) tetracyanides, and the extremely low values (*ca.* 10^{-10}) obtained with the tervalent cobalt(III) and iron(III) hexacyanides, indicate that these ions interact with the resin much less than do univalent anions of comparable polarisability.

[4] Gregor and Bregman, *J. Colloid Sci.*, 1951, **6**, 323.
[5] Bauman and Eichlorn, *J. Amer. Chem. Soc.*, 1947, **69**, 2830.
[6] Gregor, *ibid.*, 1948, **70**, 1793.
[7] Glueckauf, *Proc. Roy. Soc.*, 1952, *A*, **214**, 207.
[8] Gregor, Belle, and Marcus, *J. Amer. Chem. Soc.*, 1955, **77**, 2713.
[9] Fajans and Joos, *Z. Physik*, 1924, **23**, 46; Heydweiller, *Physik. Z.*, 1925, **26**, 526; Rogers and Malik, *J. Amer. Chem. Soc.*, 1955, **77**, 6515.
[10] Schaefer and Schubert, *Z. Physik*, 1921, **17**, 509.

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This decreased interaction of multivalent anions can be explained if the equilibrium position of the multivalent ion in the resin phase is assumed to be at the "centre of gravity" of the resin cation groups with which it is associated. This would normally cause the average distance between the resin sites and the multivalent anion to be greater than that between a resin site and a univalent anion (which would presumably be equal to the a° distance of the Debye–Hückel theory) and this is the probable cause of the reduced interaction and the lower selectivities found for multivalent than for univalent anions, as observed qualitatively by others. For instance, Kraus and Moore [11] showed that in concentrated hydrochloric acid univalent chloride complexes were more strongly adsorbed by strong-base resins than were multivalent complex chlorides.

The significance of the wide variations in *Kd* obtained here for anions of different charge is shown by comparison with the equilibrium constants found for the exchange of cations of different valency on a sulphonic acid resin. For example, the value given for the equilibrium constant [12] in the exchange of Al^{3+} for NH_4^+ was 4·1, as compared with $7{\cdot}2 \times 10^{-4}$ for the exchange of $[Co(CN)_6]^{3-}$ for $[Au(CN)_2]^-$ now found (calculated by the method in ref. 12). The maximum difference found for the selectivity coefficients for the cations most strongly and least strongly held by the sulphonic acid exchanger was of the order of ten, irrespective of the charges of the two cations; [12] values for the selectivity coefficients as large as 10^{10} have now been obtained with anion-exchange systems. In fact small changes of *Kd* with varying ionic charge of the exchanging ions can be considered as characteristic of an ion-exchange system where coulombic forces are of chief importance, whereas large variations in *Kd* with varying ionic charge of the exchanging ions is characteristic of a system where polarisation forces are of major importance.

The high affinity of Amberlite I.R.A. 400 for the reference ion $[Au(CN)_2]^-$, and its application to the extraction of gold from cyanide liquors,[1] is due to the high polarisability and linear shape of the aurocyanide ion. With a linear ion the major axis of polarisability will be along its length, so that the polarisation forces will be concentrated in this direction. No such concentration in a given direction can take place in spherical ions such as chloride, and it is significant that all three linear ions used had a high affinity for the resin. The rapid increase in the selectivity of the resin for aurocyanide compared with ions such as chloride or bromide as the mole fraction of gold in the resin phase (X_{Au}) tends to zero (Fig. 1) is compatible with the view of Burstall *et al.*[1] that the aurocyanide loading of Amberlite I.R.A. 400 should not exceed 0·3 mequiv./g. of resin (*i.e.*, $X_{Au} = 0{\cdot}1$) if base metals are to be selectively eluted before gold.

Now if the resin sites and the adsorbed anions interact through polarisation forces, then the greater the degree of interaction the smaller will be the effective concentration of free ions in the resin phase. As the degree of swelling of a resin in contact with an aqueous solution is proportional to the concentration of free ions in the resin phase, as is apparent from the Donnan membrane equilibrium, then the swelling obtained with different ionic forms of the resin in equilibrium with solutions of equivalent concentrations will vary inversely with the polarisability of the ion. Support for this comes from the data given by Gregor, Belle, and Marcus [13] for the stoicheiometric molalities (*i.e.*, molalities per 1000 g. of water in the resin phase) for various univalent ions adsorbed on a strong-base polystyrene resin containing 8% of divinylbenzene from 0·01N-equilibrating solutions. When these molalities are plotted against their ionic refractivities straight lines are obtained (Fig. 3). The halide ions lie on one straight line with nitrate, hydroxide, and thiocyanate near, but significantly off, the curve, thus again illustrating the effect of ionic shape on the polarisation forces. Perchlorate lies considerably above the halide line, thus confirming the exceptionally high polarisation forces existing between a tetrahedral ion and an anionic resin. Acetate and the three chloro-acetates lie along a second straight line, whilst

[11] Kraus and Moore, *J. Amer. Chem. Soc.*, 1951, **73**, 10.
[12] Kressman and Kitchener, *J.*, 1949, 1208.
[13] Gregor, Belle, and Marcus, *J. Amer. Chem. Soc.*, 1954, **76**, 1984.

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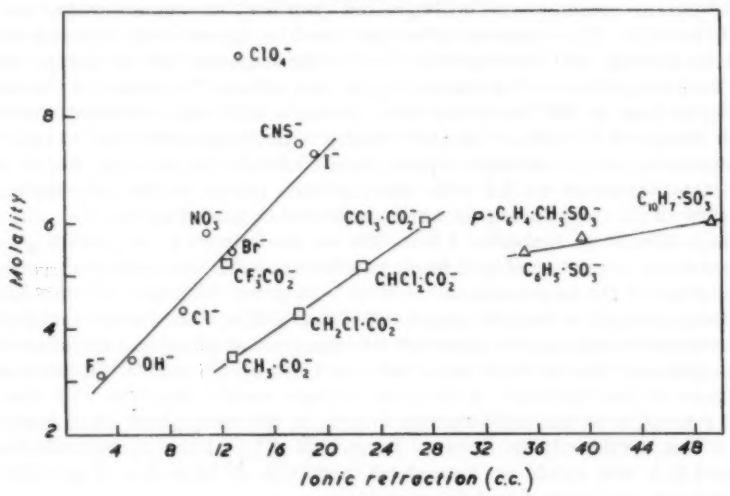
benzenesulphonate, toluene-*p*-sulphonate, and β-naphthalenesulphonate fall along a third. Trifluoroacetate, however, falls on the halide curve. The fact that three separate straight lines are obtained indicates that the degree of interaction between the charged resin sites and the adsorbed ions is affected by both the shape of the ion and its chemical nature as well as by its polarisability. With β-naphthalenesulphonate, for example, most of the measured refractivity is due to the organic part of the molecule, so that the anion might not be expected to be so greatly affected by a charged resin site as would a purely inorganic anion. This effect appears to be general, increase in the purely organic content of the adsorbed anion moving the stoicheiometric molality–refractivity curves to the right and decreasing their slope, *i.e.*, showing a decreased interaction between the resin sites and the adsorbed anions at any given value of the refractivity of the adsorbed anion.

Weak-base Resins.—Preliminary experiments with a weak-base resin (J.A. 1) containing

FIG. 3.



benzyldimethylamine groups, with solutions containing potassium auro- and argento-cyanides (*ca.* 10^{-3}M) and 0·003M-potassium cyanide (pH 10·3), gave a mean value for the selectivity coefficient K_{Ag}^{Au} of 8·3. This is very near the value found with Amberlite I.R.A. 400 at low gold loadings (Fig. 1), and suggests that the selectivity coefficients obtained for exchange of univalent anions are approximately the same on a weak-base as on a strong-base resin. This is expected, as a univalent anion can approach a resin site until it reaches the equilibrium $a°$ distance, irrespective of the spacing of the active groups in the resin matrix. However, owing to the low degree of ionisation of a weak-base resin in alkaline solution, and also to the prevention of "clustered" ionisation by the inductive effect, the resin sites will be widely spaced throughout the resin matrix, so that multivalent anions, on the assumption that they come to their equilibrium position at the "centre of gravity" of the ionised resin sites, will be more distant from these resin sites than they would be in a strong-base resin. The tendency for the displacement of multivalent by univalent anions from a weak-base resin in alkaline solution will thus be greater than with a strong-base resin in a similar environment.

The greater selectivity of weak-base resins for aurocyanide over the multivalent base-metal cyanides in alkaline cyanide media than of Amberlite I.R.A. 400 (see ref. 2) is considered to be mainly due to the mass-action effect due to the decreased resin capacity

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(see p. 239) and the increased value of the selectivity coefficients for gold displacing base-metal cyanides from the resin due to the decreased number of resin sites available for exchange as discussed above.

Low-capacity Strong-base Resins.—The selectivity for aurocyanide in alkaline cyanide solution containing multivalent base-metal cyanides is relatively greater for a weak-base than for a strong-base resin owing to the fewer resin sites available in the former under these conditions. If this explanation is correct the selectivity for gold should be similarly increased simply by reducing the capacity of a strong-base exchanger. In order to test this postulate a series of strong-base resins was prepared with capacities ranging from 0·8 to 4·5 mequiv./g. of dry chloride form and containing either 2% or 8% of divinylbenzene as cross-linking agent. Also included in the Table 2 are the volumes of 1 g. of the chloride form of the resin when loaded with complex metal cyanides and the capacity of the resin per c.c. of this final loaded form. The loadings of gold and base metals in Table 2 were obtained by treating 1 g. columns of resin with a solution containing 6 mg. of Au, 50 mg. of Ni^{II}, 30 mg. of Cu^{I}, 24 mg. of Fe^{II} (all as complex cyanides), 150 mg. of sodium cyanide, and 160 mg. of sodium thiocyanate per litre, the technique previously described [2] being used.

TABLE 2. *Adsorption of gold and base-metals from cyanide solutions by strong-base resins of various capacities.*

Resin	Divinyl-benzene (%)	Capacity (mequiv./g.) in dry chloride form	Volume of 1 g. of Cl-form of resin when loaded with complex cyanides (c.c.)	Capacity per c.c. of resin when loaded with complex cyanides (mequiv.)	Metal loading in mg./g. of dry Cl-form			
					Au	Ni	Cu	Fe
AX 15	8	0·87	1·03	0·845	6·7	15·0	3·3	0·9
AX 18	8	1·62	1·25	1·29	8·7	32·5	6·0	3·0
AX 19	8	3·56	1·48	2·40	8·7	67·5	9·6	10·0
AX 21	2	0·96	1·10	0·87	4·2	14·0	2·0	1·6
AX 22	2	1·76	1·37	1·28	4·5	33·0	5·7	4·5
AX 23	2	2·30	1·40	1·65	6·0	40·0	6·9	5·7
AX 24	2	4·46	1·42	3·15	11·3	72·5	11·3	24·1

Table 2 shows that some selectivity for aurocyanide is obtained, although the total gold loadings are not so high as on weak-base resins.[2] A more rigid interpretation of the data in Table 2 is given below.

For the displacement of a bivalent anion (B^{2-}) from a strong-base resin by aurocyanide the following equation can be written, the solution phase being assumed dilute

$$\frac{[Au(r)]^2[B^{2-}(s)]}{[Au(s)]^2[B^{2-}(r)]} = K^\circ \cdot \frac{fB(r)}{[fAu(r)]^2} = Kdm \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where the terms in square brackets refer to molarities in the resin phase (*i.e.*, moles/l. of swollen resin) and in solution, $fB(r)$ and $fAu(r)$ are the molar activity coefficients of B^{2-} and $[Au(CN)_2]^-$ in the resin phase, K° is the thermodynamic equilibrium constant, and Kdm is the molar selectivity coefficient. Molarities in the resin phase, rather than molalities, are used here as it is now the volume characteristics of the system which are being considered.

For a given resin, in this case Amberlite I.R.A. 400, $\log K'd$ is proportional to the ionic refraction of the ion being displaced from the resin by the reference ion, aurocyanide. We are now considering the displacement of a bivalent ion B^{2-} by the univalent aurocyanide ion. If we assume $K'd$ and Kdm to be simply related, $\log_{10}Kdm$ will be directly proportional to the ionic refraction of B^{2-} and hence to its polarisability. Thus

$$\log_{10}Kdm = b' - a'[R] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

where b' and a' are constants and $[R]$ is the ionic refraction of B^{2-}. If, however, we study a specific exchange so that $[R]$ remains constant but vary the capacity of the resin in order to alter the distance d between the bivalent ion and the resin sites, and hence both the total polarisation forces acting on the ion and the interaction energy between the resin sites and the ion, we can write eqn. (3) as

$$\log_{10} Kdm = b - aP \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

where P is the energy of interaction between the charged resin sites due to the polarisation forces and will vary inversely as the fourth power of the distance d between them,[14] and a and b are constants. Now d will be proportional to the distance d^1 between adjacent

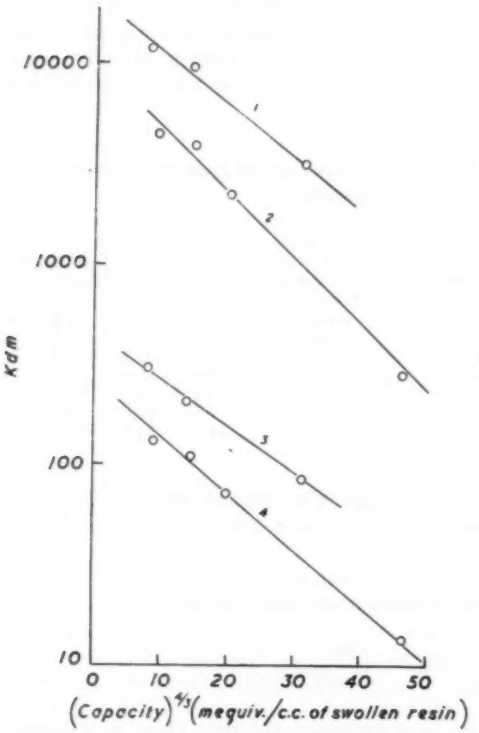

FIG. 4.

1. $Kdm_{Cu}^{Au} \times 10^{-6}$, 8% divinylbenzene.
2. $Kdm_{Cu}^{Au} \times 10^{-6}$, 2% ,,
3. $Kdm_{Ni}^{Au} \times 10^{-1}$, 8% ,,
4. $Kdm_{Ni}^{Au} \times 10^{-1}$, 2% ,,

resin sites, d^1 itself being proportional to the cube root of the resin capacity on a volume basis. Thus $P \propto 1/d^4$ so

$$P \propto (\text{Capacity})^{\frac{4}{3}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

and on substituting in eqn. (4) we get

$$\log Kdm = b - E\,(\text{Capacity})^{\frac{4}{3}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

The molar selectivity coefficient Kdm should thus vary logarithmically with the $\frac{4}{3}$ root of the resin capacity on a volume basis. Values of Kdm, calculated from Table 2, are

[14] Hirschfelder, Curtiss, and Bond, "Molecular Theory of Gases and Liquids," John Wiley and Sons, New York, 1954.

thus plotted in Fig. 4. The approximate linearity of the plots for resins with the same degree of cross-linking is strong evidence that the greater selectivities of weak-base resins for aurocyanide in alkaline cyanide solution than of a normal strong-base resin, are largely due to the smaller number of resin sites available (decreased charge density of the resin) in the former.

The selectivity shown for aurocyanide by weak-base resins in alkaline solution, and for aurocyanide by low-capacity strong-base resins, is due to aurocyanide's being univalent and able to interact strongly with the resin sites irrespective of their distribution in the resin matrix. Similar more selective behaviour would be shown by these resins for any univalent anion than for multivalent anions, although the effect is magnified with aurocyanide owing to its naturally high affinity for the resin. This selectivity for univalent anions will only be exhibited by weak-base resins in alkaline media when they will be only slightly ionised. They will not be selective in acid solution when they will be fully ionised and thus resemble a normal strong-base resin. The low-capacity strong-base resins, however, will be more selective for univalent than for multivalent ions in both acid and alkaline media. For example, a low-capacity strong-base resin should be selective for per-rhenate (which has a high affinity for the resin, see Fig. 1) in acid solution, whereas a weak-base resin would not.

In addition to the effect of charge density upon selectivity, the actual ratio of gold to multivalent base-metal cyanide on a resin will vary on altering the capacity, even though *Kd* for the exchange may remain constant. Thus it is well known that for exchange between ions of different charge the position of equilibrium, that is, the ratios of the molarities of the two ions in the resin phase, depends not only on the molarities in solution, but also on the total solution concentration. The effect of diluting the aqueous phase is to cause more of the ion of higher valency to pass into the resin. Similarly dilution of the resin phase (*i.e.*, decrease in the capacity) will cause more of the ions of the lower valency to pass into the resin with an apparent increase in selectivity, although, other factors being equal, *Kd* for the reaction will remain constant. This effect is usually referred to as the " mass action " effect.

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49. *The Ionisation of Triphenylmethyl Chloride in Nitromethane.*

By Y. Pocker.

The work of A. G. Evans and his co-workers on the ionisation of triphenylmethyl chloride is revised. Triphenylmethyl chloride, on dissolving in nitromethane, instantaneously develops hydrogen chloride to an extent determined by a simple equation of mass-law type. The hydrogen chloride contributes significantly to the electrical conductance of these solutions, and is concerned with the development of colour.

The addition of tetraethylammonium chloride completely discharges the colour associated with the carbonium ion, whilst the corresponding perchlorate has no effect. The colour discharge by added chloride ions, taken in conjunction with the experimental observations of Evans *et al.*, indicates that the ionised triphenylmethyl chloride in nitromethane is in the form of free ions, rather than ion-pairs, though the chloride ion is largely combined in, or with, hydrogen chloride.

When triphenylmethyl chloride dissolves in nitromethane, the characteristic greenish-yellow colour of the carbonium ion appears to be produced instantaneously. Bentley, A. G. Evans, and Halpern showed [1a] that the ratio of coloured to colourless material is constant, independent of stoicheiometric concentration, so they concluded that the colour arises from the conversion of a small portion of solute molecules into ion-pairs:

$$Ph_3CCl \rightleftharpoons Ph_3C^+Cl^-;\ K = [Ph_3C^+Cl^-]/[Ph_3CCl]$$

Evans *et al.* developed this further in relation to the effects of substituents on the energetics of this ionisation by use of different triarylmethyl chlorides in various nitroalkanes.[1b–1e]

Formation of Hydrogen Chloride.—When triphenylmethyl chloride dissolves in nitromethane some hydrogen chloride appears to be produced instantaneously (Table 1), in addition to the greenish-yellow colour of the carbonium ion. The optical density of such solutions remained constant for at least one day, notwithstanding the presence of hydrogen chloride. On very long standing in stoppered containers (for about six months) at room temperature, the nitromethane slowly disproportionates to give a white crystalline precipitate, identical with that obtained on leaving dry hydrogen chloride in nitromethane—it is most probably hydroxylamine hydrogen dichloride.

Table 1. *The amounts of hydrogen chloride present in freshly prepared solutions of triphenylmethyl chloride in nitromethane at* 25·0°.

$10^3[Ph_3CCl]$	120	90·0	60·0	30·0	15·0	15·0	10·0	7·5	3·25
$10^4[HCl]$	25·5	22	18	12·7	8·8	9·0	7·2	6·25	4·0
10^4k_a	5·52	5·51	5·57	5·66	5·49	5·74	5·58	5·67	5·61

The observed constancy in the $[HCl]^2/[Ph_3CCl]$ (bottom row) ratio strongly suggests that hydrogen chloride is formed *via* a route of the type:

$$(a)\ Ph_3CCl + CH_3{\cdot}NO_2 = X + HCl;\ K_a = [HCl]^2/[Ph_3CCl]$$

The nature of X has not yet been established, but it might be the triphenylmethyl ester of *aci*-nitromethane.

[1] (*a*) Bentley, Evans, and Halpern, *Trans. Faraday Soc.*, 1951, **47**, 711; (*b*) Evans, Price, and Thomas, *ibid.*, 1954, **50**, 568; (*c*) Evans, Jones, and Osborne, *ibid.*, 1954, **50**, 16, 470; (*d*) *idem*, *J.*, 1954, 3803; (*e*) Bayles, Evans, and Jones, *ibid.*, 1957, 1020.

Spectrophotometric measurements, similar to those of Evans and his co-workers,[1a-1c] indicate (Table 3) that triphenylmethyl chloride in nitromethane at 25·0° is ionised to an extent of 0·027%, independently of concentration. A 0·010M-solution has an initial specific conductance, $\kappa = 0{\cdot}185 \times 10^{-5}$ ohm^{-1} cm.$^{-1}$ at 25·0°, when water is rigorously excluded. Conductance registers free ions as opposed to ion-pairs and molecules. If diagnostic, the conductivity test would have indicated a dissociation of about 0·155% to free ions. However, there is no real discrepancy here, since this solution is 0·00072M in hydrogen chloride. An independent test shows that 0·00072M-hydrogen chloride in nitromethane has a specific conductance $\kappa = 0{\cdot}150 \times 10^{-5}$ ohm^{-1} cm.$^{-1}$, so that the specific conductance due to dissociated triphenylmethyl chloride is $0{\cdot}035 \times 10^{-5}$ ohm^{-1} cm.$^{-1}$. The equivalent conductance Λ of many tetra-alkylammonium halides at high dilution [5] is about 120 ohm^{-1} cm.^{2} mole^{-1}; using this value one obtains $2{\cdot}9 \times 10^{-6}$ mole l.$^{-1}$ as the concentration of dissociated triphenylmethyl chloride and the extent of ionisation as 0·029%, in good agreement with the spectrophotometric value.

Effects of Added Tetra-alkylammonium Salts.—According to the ion-pair hypothesis suggested by Evans and his co-workers, solutions of triphenylmethyl chloride in nitromethane should show no " common-ion " depression of the ionisation when a saline chloride is added. However, added tetraethylammonium chloride discharges the colour of the carbonium ion, whilst the perchlorate has no observable effect on the colour. The results are summarised in Table 2 where the calibration of colour in terms of the concentration of triphenylcarbonium ion, $[Ph_3C^+]$, is made on the assumption [1a-c] that the extinction coefficient of the carbonium ions in nitromethane is the same as in 98% sulphuric acid, where triphenylmethanol is taken to be completely ionised.[2a, b, 3]

TABLE 2. *The effect of added tetra-alkylammonium salts on solutions of triphenylmethyl chloride in nitromethane*; $[Ph_3CCl] = 0{\cdot}0150$ *and contains* $8{\cdot}8 \times 10^{-4}$M-HCl.

$10^5[NEt_4Cl]$	$10^4[Ph_3C^+]$ (g.-ions l.$^{-1}$)	$10^3[NEt_4ClO_4]$	$10^4[Ph_3C^+]$
None	4·0	1	4·0
0·75	3·2	2·5	4·0
7·5	0·82	5·0	4·0
75	<0·02		
750	Indistinguishable experimentally at 430 mμ from pure nitromethane		

The following salts (0·001M) reduced the concentration of spectrophotometrically observable carbonium ions to 1% or less of the original: $Bu^n_4NN_3$, NEt_4NO_2, NEt_4F, $NEt_4O{\cdot}COCH_3$, $NEt_4O{\cdot}COPh$, $NEt_4O{\cdot}CO{\cdot}C_6H_4{\cdot}NO_2$ (*p*).

In contrast to the perchlorate the anions which discharge the colour are derived from acids weaker than hydrogen chloride, and so they liberate chloride ions from undissociated hydrogen chloride. Also, in contrast to the perchlorate, these anions can capture the carbonium ions more efficiently than do chloride ions, leading to products which dissociate negligibly in nitromethane. In addition, the liberated chloride ions would further suppress the concentration of carbonium ions by a mass-law effect.

Nature of Equilibrium.—Evans and his co-workers' observations cannot accommodate a simple equilibrium between molecules and free ions, but their ion-pair hypothesis cannot account for the observed chloride-ion effect. This dilemma can be resolved if one takes into account that hydrogen chloride is present in much larger concentration than the triphenylcarbonium ions and also that the hydrogen dichloride ion is stable in nitromethane.*

* Smith and Hammett (*J. Amer. Chem. Soc.*, 1945, **67**, 23) measured the acidity function H_0 of sulphuric acid and hydrogen chloride in nitromethane and had to postulate what they described as new and unexpected effects on the activity coefficients. As far as can be seen from their figures, ionisation schemes similar to the ones now suggested for the acid would fit the results.

[2] (*a*) Hantzsch, *Z. phys. Chem.*, 1908, **61**, 257; (*b*) *idem*, *Ber.*, 1922, **55**, 953.
[3] Hammett and Deyrup, *J. Amer. Chem. Soc.*, 1933, **55**, 1900.

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The following three equilibria are considered

(1) $HCl \rightleftharpoons H^+ + Cl^-$; $K_1 = [H^+][Cl^-]/[HCl]$

(2) $Cl^- + HCl \rightleftharpoons HCl_2^-$; $K_2 = [HCl_2^-]/([Cl^-][HCl])$

(3) $Ph_3CCl \rightleftharpoons Ph_3C^+ + Cl^-$; $K_3 = [Ph_3C^+][Cl^-]/[Ph_3CCl]$

In the absence of added chloride ions, $[HCl_2^-] > [Cl^-]$, *i.e.*, $K_2 > K_1$. In the region where $[H^+] > [Ph_3C^+]$ one obtains $[H^+] \approx [HCl_2^-]$.

Then from equilibria (1) and (2)

$$K_1K_2 \approx [H^+]^2/[HCl]^2 \approx [HCl_2^-]^2/[HCl]^2 \text{ and } [Cl^-] \approx \sqrt{(K_1/K_2)}$$

Thus equilibria (1) and (2) act as a " buffer " with respect to chloride ions, keeping the latter approximately * constant. Hence

$$K_3 \approx [Ph_3C^+]/[Ph_3CCl] \cdot \sqrt{(K_1/K_2)}$$

Two additional ionisation schemes involving electrophilic catalysis, (3*a*) and (3*b*), are derivable from previous equilibria:

(3*a*) $Ph_3CCl + H^+ = Ph_3C^+ + HCl$; $K_{3a} = [Ph_3C^+][HCl]/([Ph_3CCl][H^+]) \approx [Ph_3C^+]/[Ph_3CCl] \cdot 1/\sqrt{(K_1K_2)}$

(3*b*) $Ph_3CCl + HCl = Ph_3C^+ + HCl_2^-$; $K_{3b} = [Ph_3C^+][HCl_2^-]/([Ph_3CCl][HCl]) \approx [Ph_3C^+]/[Ph_3CCl] \cdot \sqrt{(K_1K_2)}$

The equilibrium constants K_3, K_{3a}, and K_{3b} agree with the experimental findings of Evans and his co-workers and with the salt effects now observed, but are independent of the way in which hydrogen chloride is originally produced.

In benzene solution, a necessary elaboration of kinetic [4c] and thermodynamic [4a] schemes is the explicit recognition of an ion-pair form. No such elaboration is necessary with regard to the thermodynamic equilibria governing the spectrophotometrically observable triphenylcarbonium ions present in solutions of triphenylmethyl chloride in nitromethane, with its relatively high dielectric constant. On the other hand, specific interaction of chloride ions with the hydrogen chloride present in such solutions plays an important rôle.

Experimental

Materials.—Special care was taken to purify the starting materials. No method was found to purify commercial triphenylmethyl chloride for use as starting point for the preparation of spectrophotometrically satisfactory samples, even though it could be easily purified to have the correct m. p., give good analtytical data, and afford reproducibility in measurements within a given batch. It was therefore prepared as described previously.[4b]

Commercial nitromethane was refluxed under nitrogen with activated charcoal and dried ($CaCl_2$, then P_2O_5) with filtration after each stage. It was fractionated (b. p. 100·5—101·0°), passed through a column of freshly dried chromatographic alumina, then again fractionated, and passed through alumina. The nitromethane so obtained was tested for traces of acids and aldehydes and was gas-chromatographed. Its specific conductance was $0{\cdot}132 \times 10^{-7}$ ohm^{-1} cm.$^{-1}$ at 25·0°.[5]

* A rigorous calculation by use of (1), (2), and the charge-balance relation $[Ph_3C^+] + [H^+] = [HCl_2^-] + [Cl^-]$ gives

$$[Cl^-] = \sqrt{(K_1/K_2)} \cdot \sqrt{\{([H^+] + [Ph_3C^+] - [Cl^-])/[H^+]\}}$$

This relation shows that even when $[H^+]$ is only moderately large relative to $[Ph_3C^+]$, one obtains $[Cl^-]$ approximately constant.

[4] (*a*) de la Mare, Hughes, Ingold, and Pocker, *J.*, 1954, 2930; (*b*) Hughes, Ingold, Patai, and Pocker, *J.*, 1957, 1206; (*c*) Hughes, Ingold, Mok, Patai, and Pocker, *ibid.*, p. 1220; (*d*) *idem*, *ibid.*, p. 1265.

[5] Wright, Murray-Rust, and Hartley, *ibid.*, 1931, 199.

Tetra-alkylammonium salts were prepared and purified as described previously.[4a, c]

TABLE 3. *Triphenylcarbonium-ion concentration in nitromethane solutions of triphenylmethyl chloride at* 25·0°; $K = [Ph_3C^+]/[Ph_3CCl]$.

$10^2[Ph_3CCl]$	6·0	5·0	4·0	3·0	2·0	1·5	1·0
$10^6[Ph_3C^+]$ (g.-ions $l.^{-1}$)	16·1	13·4	10·8	8·0	5·3	4·0	2·67
10^4K	2·68	2·68	2·70	2·665	2·65	2·66	2·67

Spectrophotometry.—The optical density of nitromethane solutions of triphenylmethyl chloride was determined on a Unicam spectrophotometer at 430 mμ.[4a-c] Details of some measurements are given in Table 3, where the calibration of colour in terms of $[Ph_3C^+]$ is as discussed previously.

Acid Determinations.—Aliquot portions removed from freshly prepared solutions were quenched in cool dry benzene and titrated quickly with 0·001M- and 0·005M-triethylamine in benzene, bromophenol-blue being the indicator. Some samples were quenched in a benzene solution of triethylamine and titrated with dry hydrogen chloride in ether. The results of this method were the same. The titratable acid was shown to be hydrogen chloride by pumping off freshly prepared solutions, isolating the vapour in a cold trap, and analysing it for acidity and chloride.

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50. *Kinetics of the Reaction between 2-Ethoxycarbonyl-2-iodocyclohexanone and Iodide Ions.*

By R. P. BELL and D. C. VOGELSONG.

Measurements are reported of the rate of the reaction of 2-ethoxycarbonyl-2-iodo*cyclo*hexanone with iodide ions over a range of hydrogen-ion concentrations. The pK of 2-ethoxycarbonyl*cyclo*hexanone and the equilibrium percentage of enol in its aqueous solutions have also been determined. By combining these results with the equilibrium constant for the iodination of 2-ethoxycarbonyl*cyclo*hexanone, velocity constants are derived for the fast reactions of iodine and tri-iodide ions with the enol and the anion of the ester.

BELL and ENGEL [1] studied the kinetics of the reaction between ethyl iodomalonate and iodide ions, and showed that the results could be used to deduce the velocities of the very fast reactions of iodine and tri-iodide ion with the enol and anion of malonic ester. It was necessary to know the equilibrium constant for the iodination reaction, the acid dissociation constant of malonic ester, and the equilibrium percentage of enol in aqueous solution, of which the last two could only be estimated roughly. The present paper describes similar measurements with 2-ethoxycarbonyl*cyclo*hexanone. Although this compound is experimentally somewhat less convenient than malonic ester, it has the advantage that the acid dissociation constant and the percentage of enol can be measured directly, and hence reliable values can be obtained for the velocity constants of the iodination reactions. The reaction between the iodo-ester (RI) and iodide ions was studied in presence of ascorbic acid, which removes the iodine produced and renders the reaction irreversible. Bell and Engel [1] showed that under these conditions the kinetics are represented by

$$\frac{1}{[RI]} \cdot \frac{d[RI]}{dt} = [I^-]\left\{K_{RH}(k_2 + k_2'K_I[I^-]) + K_E\,[H^+](k_3 + k_3'K_I[I^-])\right\}/K \quad . \quad (1)$$

[1] Bell and Engel, *J.*, 1957, 247.

where, if RH and HR represent the keto and enol form of the ester, the equilibrium constants are given by

$$K_{RH} = [H^+][R^-]/[RH], \qquad K_E = [HR]/[RH],$$
$$K = [RI][I^-][H^+]/[RH][I_2], \text{ and } K_I = [I_3^-]/[I_2][I^-],$$

and the second-order velocity constants correspond to the following reactions:

$$HR + I_2, k_2 \qquad HR + I_3^-, k_2' \qquad R^- + I_2, k_3 \qquad R^- + I_3^-, k_3'$$

If, as in our measurements, $[I^-]$ and $[H^+]$ are constant during an experiment, then the left-hand side of eqn. (1) represents a first-order velocity constant for that experiment.

Experimental

2-Ethoxycarbonyl*cyclo*hexanone (subsequently referred to as " ester ") was redistilled *in vacuo* (109°/12 mm.) and its aqueous solutions were not kept for more than a few hours before use. Solutions of ascorbic acid were made from B.D.H. (−)-ascorbic acid, protected from the light, and used on the day of preparation. All other solutions were prepared from AnalaR materials, and all water used had been re-distilled in glass.

The general procedure in the kinetic experiments followed that described by Bell and Engel, but the greater velocities and higher value of K limited the range of concentrations of iodide and of hydrogen ion which could be studied. A solution of ester *ca.* 0·002M was partly iodinated in an acetate buffer solution, and brought to 25°. To this was added rapidly a solution of potassium iodide containing sufficient ascorbic acid to react with part of the iodine produced, and the time for the first appearance of free iodine was detected by the depolarization method.[1] Because of the high value of K and the low solubility of the iodo-ester it was necessary to detect very low concentrations of iodine, and the sensitivity of the method was increased by using platinum gauze in place of wire electrodes. By repeating this procedure with varying quantities of ascorbic acid five points were obtained for each value of $[I^-]$ and $[H^+]$, and the first-order velocity constant obtained from the linear plot of log [RI] against time. These constants are listed in the Table.

In all the reaction mixtures the ionic strength was made up to 0·2 by the addition of potassium chloride. In calculating the hydrogen-ion concentration of the buffer solutions the value $f_\pm^2 = 0{\cdot}6$ was taken for the activity coefficient factor at $I = 0{\cdot}2$ (ref. 2).

The acid dissociation constant of the ester was determined at 25° by measuring the pH of partly neutralized solutions of ester, with a Cambridge pH meter and an " Alki " glass electrode, calibrated with 0·05M-borax solution. The solutions were made up to an ionic strength of 0·2 with potassium chloride. The observed pH changed slowly with time, probably because of hydrolysis of the ester, but could be extrapolated back to zero time. In calculating the thermodynamic value of pK it was again assumed that $f_\pm^2 = 0{\cdot}6$. Successive experiments with degrees of neutralization between 0·25 and 0·60 gave pK (thermodynamic) = 10·94, 11·01, 10·94, 10·85; mean 10·94.

In determining the equilibrium proportion of enol in aqueous solution, ester solutions were kept at 25° for 19 hr. in acetate buffer solutions with $[OAc^-] = 0{\cdot}08$ and [HOAc] between 0·005 and 0·24. The concentration of ester was throughout about 0·001M. According to Bell and Goldsmith's kinetic measurements[3] the half-time for reaching enolization equilibrium in these solutions should be less than 1 hr. The acetate ions were then neutralized by a slight excess of hydrochloric acid, and the enol estimated by rapid titration with 0·001M-bromine in 1M-potassium bromide, the depolarization method being used for detecting the first appearance of free bromine. According to Bell and Goldsmith the half-time for enolization in these slightly acid solutions is 20 hr., and in fact reproducible results were obtained, successive experiments giving for the enol content 2·05, 1·97, 1·99, 2·00, and 2·17%: mean 2·04% of enol.

[2] Larsson and Adell, *Z. phys. Chem.*, 1931, **156**, 352.
[3] Bell and Goldsmith, *Proc. Roy. Soc.*, 1952, *A*, **210**, 322.

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Apparent first-order velocity constants (10^4k; k *in sec.*$^{-1}$) *for reaction of iodo-ester with iodide ions at* 250°. (*The corresponding calculated values are given in parentheses.*)

10^4[I$^-$]: / 10^2[H$^+$]	206	307	406	506
146	67 (70)	115 (121)	173 (180)	243 (250)
296	107 (103)	178 (173)	260 (255)	351 (351)
413	131 (130)	219 (217)	322 (317)	442 (434)
583	172 (168)	281 (278)	410 (402)	563 (551)
876	231 (233)	382 (383)	536 (554)	724 (750)

Discussion

The calculated velocity constants in the Table are obtained from the expression

$$k = 0{\cdot}106[I^-] + 3{\cdot}77[I^-]^2 + 8{\cdot}91 \times 10^3[H^+][I^-] + 9{\cdot}17 \times 10^4[H^+][I^-]^2 \quad . \quad (2)$$

where the numerical coefficients were obtained graphically from the experimental results by using either plots of $k/[I^-]$ against $[H^+]$ at constant values of $[I^-]$, or of $k/[I^-]$ against $[I^-]$ at constant values of $[H^+]$. The observed and calculated values of k agree within experimental error, and since all the terms in eqn. (2) contribute appreciably to the velocity the four numerical coefficients are all known to better than about $\pm 10\%$. As in the work of Bell and Engel [1] the rate law corresponds to eqn. (1), and the results can be used to derive the velocity constants of the fast halogenation steps. Our own measurements give $K_E = 0{\cdot}0204$, and $K_{RH} = 1{\cdot}15 \times 10^{-11}/f_\pm^2 = 1{\cdot}9 \times 10^{-11}$ at $I = 0{\cdot}2$. Similarly, from Bell and Gelles's measurements [4] we have $K = 0{\cdot}505/f_\pm^2 = 0{\cdot}842$, and $K_I = 714$ from Jones and Kaplan.[5] Inserting these values in eqn. (1) and (2) we find the following velocity constants:

Reaction	Velocity constant	Reaction	Velocity constant
Enol + I_2	$3{\cdot}8 \times 10^5$ l. mole^{-1} sec.$^{-1}$	Enol ion + I_2	$4{\cdot}7 \times 10^9$ l. mole^{-1} sec.$^{-1}$
Enol + I_3^-	$5{\cdot}4 \times 10^3$,,	Enol ion + I_3^-	$2{\cdot}3 \times 10^8$,,

These values are of the same order of magnitude as those derived by Bell and Engel [1] for the iodination of ethyl malonate, and also those observed directly by Bell and Spiro; [6] from the bromination of ethyl malonate at low bromine concentrations: they are, however, more reliable than any previous estimates of the halogenation velocities of enols and their ions.

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Physical Chemistry Laboratory, Oxford. [*Received, August 8th,* 1957.]

[4] Bell and Gelles, *Proc. Roy. Soc.*, 1952, *A*, **210**, 310.
[5] Jones and Kaplan, *J. Amer. Chem. Soc.*, 1928, **50**, 1845.
[6] Bell and Spiro, *J.*, 1953, 429.

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51. *Kinetics and Mechanism of Aromatic Halogenation by Hypohalous Acids. Part III.* Chlorination of* p-*Anisic Acid by Hypochlorous Acid in* 75% *Acetic Acid.*†

By G. Stanley and J. Shorter.

Measurements of initial rate of reaction at 20° have been made for the chlorination by hypochlorous acid of *p*-anisic (*p*-methoxybenzoic) acid in aqueous acetic acid containing 75% (w/w) of acetic acid. The dependence of rate on the concentrations of hypochlorous acid c_1 and anisic acid c_2 is given by $r_0 = Ac_1c_2/(1 + Bc_1)$, where A and B are constants. The initial rate is virtually independent of the hydrogen-ion concentration, for the influence of acids on r_0 is comparable with that of their sodium salts.

These results are interpreted in terms of reaction between a non-ionic chlorinating species and an active form of the anisic acid, produced at a finite rate from the bulk form of the ether. The natures of the chlorinating species and active form are discussed. Molecular chlorine is unimportant as a chlorinating species in the absence of added chloride, the effective halogenating species probably being acetyl hypochlorite. It is suggested that there is considerable formation of unreactive complexes of aromatic ether with acetic acid, and that the active form is a hydrated anisic acid molecule.

The reaction mechanism thus differs from that of the chlorination of aromatic compounds by hypochlorous acid in water,[1,2] and from that of bromination by hypobromous acid in 75% acetic acid,[3,4] where halogen cations constitute the halogenating species.

Bradfield and Brynmor Jones and their colleagues have often studied the kinetics and mechanism of the halogenation of aromatic ethers and anilides in acetic acid. Most of this work has been concerned with chlorination by molecular chlorine in acetic acid containing 1% of water,[5] but recently Branch and Brynmor Jones[3,4] studied the bromination of aromatic ethers by hypobromous acid in aqueous acetic acid containing 75% (w/w) of acetic acid. They concluded that hypobromous acid was itself rather unreactive, and that the effective brominating species was either the solvated cation $\overset{+}{Br}OH_2$ or the free cation $\overset{+}{Br}$, present in amount controlled by the hydrogen-ion concentration through the equilibria

$$HOBr + \overset{+}{H_3}O \rightleftharpoons \overset{+}{Br}OH_2 + H_2O \; ; \; \overset{+}{Br}OH_2 \rightleftharpoons \overset{+}{Br} + H_2O$$

This is in agreement with the results of Derbyshire and Waters [6] and of Wilson and Soper [7] on the reactions of hypobromous acid with aromatic compounds in aqueous solution. Our present work on the reaction of aromatic ethers with hypochlorous acid in 75% acetic acid arose as an extension of that of Branch and Brynmor Jones. It comprises the investigation of the chlorination of nine *p*-alkoxybenzoic acids and several *para*-substituted anisoles. The arrangement of electron-attracting and -releasing groups in the molecules ensured that chlorination would occur only in one of the positions *ortho* to the alkoxyl group. Preliminary experiments showed that the kinetics were more complicated than those of bromination by hypobromous acid in 75% acetic acid, and it was decided that initial-rate

* Part II, *J.*, 1955, 2921.

† Presented in outline at the XVIth International Congress of Pure and Applied Chemistry, Paris, 1957.

[1] Derbyshire and Waters, *J.*, 1951, 73.
[2] de la Mare, Ketley, and Vernon, *J.*, 1954, 1290.
[3] Branch and Brynmor Jones, *J.*, 1954, 2317.
[4] *Idem*, *J.*, 1955, 2921.
[5] Part XVII, Brynmor Jones and Richardson, *J.*, 1955, 2772.
[6] Derbyshire and Waters, *J.*, 1950, 564.
[7] Wilson and Soper, *J.*, 1949, 3376.

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measurements provided the best means of investigation. This paper describes a detailed study of anisic (*p*-methoxybenzoic) acid, and Part IV (following paper) describes a less detailed survey of the other ethers.

Nuclear halogenation of aromatic compounds by hypochlorous acid has previously been studied. Derbyshire and Waters [1] showed that the reaction of hypochlorous acid with sodium toluene-ω-sulphonate in aqueous solution was catalysed by mineral acid and concluded that chlorine cations were the effective species. de la Mare, Ketley, and Vernon [2] studied the reactions of hypochlorous acid with aromatic compounds in water and in aqueous dioxan, in the presence of silver perchlorate to suppress the chloride-ion concentration and thus eliminate the intervention of molecular chlorine. The kinetics were complicated, but the authors showed that the mechanism involved chlorine cations. They could distinguish between the action of solvated $\overset{+}{\mathrm{ClOH}}_2$ and free $\overset{+}{\mathrm{Cl}}$ cations, the part played by each depending on the reactivity of the aromatic compound. At hypochlorous acid concentrations above 0·001M, chlorine monoxide, derived from the reversible dehydration of hypochlorous acid, was found to play a part. de la Mare, Ketley, and Vernon [8] have also shown that in solutions of hypochlorous acid in 98% acetic acid, acetyl hypochlorite is an important chlorinating species. Studies of side-chain substitution in anilides have been made by Soper and his colleagues.[9,10] Here the hypochlorite ion appears to be effective.

Addition reactions involving hypochlorous acid and unsaturated compounds such as allyl alcohol were studied by Israel [11] and by Shilov [12] and their colleagues; molecular hypochlorous acid and chlorine monoxide are important chlorinating species. Experiments carried out in the presence of sodium acetate and acetic acid buffers suggested that acetyl hypochlorite was then an important intermediate. (The participation of acyl hypohalites in the reactions of hypohalous acids with organic compounds in buffer solutions has also been suggested in connection with the iodination of phenol [13] and the bromination of aromatic compounds.[7])

Hypochlorous acid thus functions in a variety of ways in its reactions with organic compounds.

Experimental

Purification of Acetic Acid.—Acetic acid containing 2% of chromium trioxide (" AnalaR ") was distilled, then redistilled from 0·2% of naphthalene-2-sulphonic acid in the theoretical amount of " AnalaR " acetic anhydride.[14] Head and tail fractions were rejected and the final distillate had m. p. 16·5°, corresponding to 99·95% purity. The reaction medium containing 75% (w/w) of acetic acid ($n_D^{20} = 1{\cdot}3756$) was prepared by adding the calculated volume of acetic acid (after allowance for the slight water content of the purified acid) to a known volume of distilled water.

Anisic Acid.—The preparation of very pure anisic acid required for kinetic studies is difficult. The product obtained from *p*-hydroxybenzoic acid and methyl iodide by Brynmor Jones's method [15] proved unsatisfactory. Measurements of the rate of chlorination by hypochlorous acid clearly showed the presence of the more reactive *p*-hydroxybenzoic acid. Presumably loss of methyl iodide by volatilisation prevented quantitative conversion into anisic acid, and repeated crystallisation failed to remove all traces of *p*-hydroxybenzoic acid. An alternative method of preparation was therefore adopted. Anisaldehyde was prepared by treating

[8] de la Mare, Ketley, and Vernon, *Research*, 1953, **6**, 12s.
[9] Mauger and Soper, *J.*, 1946, 71.
[10] Pryde and Soper, *J.*, 1931, 1510.
[11] Israel, Martin, and Soper, *J.*, 1950, 1282; Israel, *J.*, 1950, 1286; Craw and Israel, *J.*, 1952, 550; Reeve and Israel, *J.*, 1952, 2327.
[12] Shilov and Kupinskaya, *Doklady Akad. Nauk S.S.S.R.*, 1951, **81**, 621; Shilov, *ibid.*, 1952, **84**, 1001.
[13] Painter and Soper, *J.*, 1947, 342.
[14] Orton and Bradfield, *J.*, 1927, 983.
[15] Brynmor Jones, *J.*, 1935, 1874.

p-hydroxybenzaldehyde with methyl iodide and potassium carbonate in *cyclo*hexanone,[16] and was then oxidised to anisic acid by neutral potassium permanganate. The anisic acid was recrystallised several times from acetic acid and from benzene; it had m. p. 184°, in agreement with that given by Gray and Brynmor Jones.[17] The advantage of this method is that any unmethylated hydroxy-compound remains with the insoluble inorganic matter and is removed by filtration before the *cyclo*hexanone is distilled off.

Hypochlorous Acid.—Water was saturated with chlorine from a cylinder and then shaken with silver sulphate for about ½ hr. After filtration, the aqueous solution of hypochlorous acid was distilled at *ca.* 15 mm. and 20°. The vapour of a water-bath was sufficient to heat the flask, thus preventing superheating and minimising decomposition of hypochlorous acid. Silver chloride was deposited during distillation, so it was advisable for the capillary " leak " not to extend to the base of the flask. The distillation was carried out in diffused light, but it was not found necessary to blacken the apparatus. The hypochlorous acid solutions thus obtained were about 0·05M (by iodometry) and had pH 4·2—4·4 (measured by glass electrode and Cambridge Instrument Company pH meter). From the dissociation constant of hypochlorous acid (*ca.* $3·2 \times 10^{-8}$ at 20°; see Sidgwick [18]), the pH of 0·05M-hypochlorous acid containing no other free acid should be 4·4. The product thus appeared to be of good quality. The acid was prepared daily as required.

Kinetic Measurements.—All measurements were made at 20°. Solutions of hypochlorous acid and aromatic ether in 75% acetic acid were mixed and the progress of the reaction followed by removal of samples and analysis for residual hypochlorous acid. Reaction rates were generally high and it was necessary to use an H-shaped vessel to permit rapid mixing of the reactants [3] and a special 5 c.c. pipette for sampling. The latter was of the automatic type, the filling and emptying being controlled by a tap and rubber bulb attached to the overflow bulb. The pipette was calibrated by weighing samples of 75% acetic acid.

In the kinetic experiments, aqueous hypochlorous acid was diluted with glacial acetic acid to give a solution in 75% acetic acid of concentration 1·25 times that desired in the ultimate reaction mixture. 50 c.c. of this solution were placed in one limb of the reaction vessel and 10 c.c. of ether solution (of concentration five times that desired in the reaction mixture) in the other. In most experiments the concentrations of hypochlorous acid and ether were in the range 0·004—0·01M. Two 5 c.c. samples of hypochlorous acid solution were taken from the reaction vessel and analysed by iodometry so that the initial concentration in the reaction mixture was accurately known. The remaining 40 c.c. of hypochlorous acid were rapidly mixed with the ether solution. Samples were withdrawn at intervals appropriate to the speed of the reaction and were run into excess of potassium iodide solution, previously freed from dissolved oxygen by a stream of nitrogen. This procedure stopped the halogenation of the aromatic ether, and the iodine liberated was titrated with 0·003N-sodium thiosulphate. Measurements were usually made to the stage at which 20—25% of the hypochlorous acid had reacted with the ether, about five samples being taken.

Initial rate was obtained by plotting the thiosulphate titres against the time, drawing the tangent at zero time, and measuring the slope. Rates were expressed as moles of HOCl used per litre per second. Accurate drawing of the tangent was difficult when the graph had a pronounced curvature. In such cases r_0 was also obtained by estimating the rate at fixed intervals along the graph, and extrapolating to zero time.

The Absence of Any Effect of Chloride Ion present in the Hypochlorous Acid.—de la Mare and his colleagues,[2] in their studies of the reactions between hypochlorous acid and aromatic compounds in aqueous solution, have generally added silver perchlorate to reduce the chloride-ion concentration and thereby eliminate the participation of molecular chlorine produced through the reaction $HOCl + H^+ + Cl^- \rightleftharpoons Cl_2 + H_2O$. Derbyshire and Waters [1] showed that the addition of chloride ion accelerates the chlorination of sodium toluene-ω-sulphonate by aqueous hypochlorous acid. They were satisfied, however, that chlorine produced from chloride-ion normally present as impurity was not significant. We have now shown as follows that there is no important effect of chloride impurity on the chlorination in 75% acetic acid.

The approximate concentrations of chloride ion and chlorine in 0·005M-hypochlorous acid in 75% acetic acid can easily be calculated. Freshly distilled aqueous hypochlorous

[16] Gray and Brynmor Jones, *J.*, 1954, 1467.
[17] *Idem*, *J.*, 1953, 4179.
[18] Sidgwick, " The Chemical Elements and their Compounds," Oxford, 1950, p. 1214.

acid may be taken to have a molarity of 0·05 and a pH of 4·2; the dissociation constant of hypochlorous acid is taken to be $3{\cdot}2 \times 10^{-8}$ at 20° and the hydrolysis constant of chlorine, $K_h = [HOCl][H^+][Cl^-]/[Cl_2]$, to be 3×10^{-4} (Jakowkin [19]). It is necessary to assume that this value for K_h in water may be applied to 75% acetic acid; it should not be seriously different. The hydrogen-ion concentration of 75% acetic acid enters into the calculation, and, as shown later, this may be taken as 10^{-2}. From these data the concentrations of chloride ion and chlorine in an 0·005M-hypochlorous acid in 75% acetic acid can be calculated as *ca.* 3×10^{-6} and 4×10^{-7} respectively. (The actual concentrations may well be much lower than these values, for there is probably extensive combination between the acetic acid and hypochlorous acid.) If molecular chlorine is an important chlorinating species under the ordinary conditions of the kinetic experiments, raising the chloride-ion concentration to 10^{-4} by adding sodium chloride should increase r_0 greatly. It was found, however, that 10^{-4}M-sodium chloride had no effect (Table 1), irrespective of whether the salt was dissolved in the anisic acid solution or the hypochlorous acid solution before mixing. Further, the concentration of chlorine should depend greatly on the hydrogen-ion concentration, and the absence of any great effect of hydrogen-ion concentration on the rate (see later) confirms that molecular chlorine is not normally an important chlorinating species. At concentrations of sodium chloride rather above 10^{-4}, r_0 rises steeply with chloride concentration (Table 1), presumably owing to the participation of molecular chlorine, which is evidently extremely reactive in 75% acetic acid.*

Implicit in the above considerations is the assumption that significant decomposition of hypochlorous acid does not occur between carrying out the distillation and starting the kinetic experiment, an interval of about 30 min. Hypochlorous acid may decompose according to the equations [20] $2HOCl \longrightarrow 2HCl + O_2$; $3HOCl \longrightarrow 2HCl + HClO_3$. The pH of distilled hypochlorous acid falls by only 0·01 unit in 30 minutes' standing in diffused light. Iodometric measurement of the stability of the solution in 75% acetic acid showed that a 0·007M-solution was decomposed only to the extent of about 0·2% in 30 minutes' standing in the reaction vessel. The decomposition is thus very slow and while it may well increase considerably the amount of chloride ion present, the amount produced during the time in question would not invalidate the argument.

TABLE 1. *The effect of sodium chloride.*

10^3[HOCl] (M) ...	4·81	4·81 [a]	4·81	7·26	7·26	5·25	5·25	5·25
10^4[NaCl] (M)	0	1	1	0	1	0	5	10
$10^6 r_0$	5·06	5·13	5·06	6·42	6·49	5·28	9·53	17·45

[Anisic acid] = 0·01M. *a* denotes that the sodium chloride was dissolved initially in the hypochlorous acid solution. In the other experiments the salt was dissolved in the anisic acid solution.

Further, if molecular chlorine was normally an important halogenating species, erratic results would have been obtained. The quality of the distilled hypochlorous acid as measured by pH varied; presumably this corresponded to variations in the content of hydrochloric acid. The time taken to prepare for the kinetic experiments also varied and this would have led to variations in the amount of chloride ion produced by the decomposition of hypochlorous acid. Nevertheless the results were highly reproducible and this would hardly have been so if the mechanism involved a species produced from an impurity present in varying amount.

DISCUSSION

Dependence of r_0 on Concentrations of Anisic Acid and Hypochlorous Acid, and the Effects of Sodium Salts and of Acids in 75% Acetic Acid at 20°.—Initial rate is directly proportional to the concentration of anisic acid in the range 0—0·01M (Figure). At very low concentrations the rate is proportional to the concentration of hypochlorous acid, but

* Branch and Brynmor Jones [3] found that molecular bromine and bromine monochloride were very unreactive towards aromatic ethers in 75% acetic acid. This low reactivity was confirmed here; the addition of an excess of bromide ion to convert the hypochlorous acid completely into bromine monochloride and bromine virtually stopped the halogenation of anisic acid.

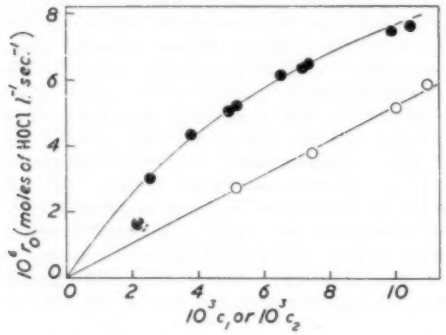
[19] Jakowkin, *Z. phys. Chem.*, 1899, **29**, 613.
[20] Sidgwick, ref. 18, p. 1215.

at higher concentrations the order of reaction falls. A possible relation to express this behaviour is:

$$r_0 = Ac_1c_2/(1 + Bc_1) \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where c_1 is the concentration of hypochlorous acid, c_2 that of anisic acid, and A and B are constants. If this relation is valid the graph of $1/r_0$ against $1/c_1$ (c_2 being constant) should be linear. This is found to be so, and, from the slope and intercept, A and B are 0·155 and 102 respectively. The dependence of r_0 on c_1, when $c_2 = 0{\cdot}01$, given by expression (1) with these values of A and B, is shown by the curve in the Figure. The agreement with experiment is satisfactory.

Similar behaviour was found with reaction solutions that were 0·1M in sodium acetate or nitrate, and was also found for other *p*-alkoxybenzoic acids and for methyl anisate and *p*-chloroanisole (Part IV, following paper).



The dependence of initial rate r_0 on anisic acid concentration c_2 and hypochlorous acid concentration c_1.

○ $c_1 = 0{\cdot}00505$M (range 0·00504—0·00506). c_2 varying.

● $c_2 = 0{\cdot}01$M. c_1 varying.

The simplest interpretation of these results is that the mechanism involves a chlorinating species reacting with an active form of anisic acid, produced from unreactive bulk form at a finite rate, as in the following scheme:

$$\underset{c_2}{E_b} \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \underset{c_3}{E_a} \qquad\qquad E_a + D \xrightarrow{k_3} \underset{c_3 \quad fc_1}{\text{product}}$$

E_b represents the bulk form and E_a the active form of anisic acid. D is the chlorinating species, assumed present in concentration proportional to that of hypochlorous acid as determined by iodometry, f being the proportionality constant.

If the concentration of E_a be assumed to reach a small stationary value at the start of the kinetic experiment, then

$$r_0 = (k_1k_3f/k_2)c_1c_2/[1 + (k_3f/k_2)c_1] \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

which is expression (1) with $A = k_1k_3f/k_2$ and $B = k_3f/k_2$.

The effects of various salts and of acids on r_0 are shown in Tables 2—5. The effects of sodium salts are complex, and specific to the anion. 0·025M-Sodium nitrate raises r_0 by about 20% (Table 2), but the addition of salt up to 0·1M has little further effect. Very low concentrations of sodium perchlorate and sodium hydrogen sulphate (Tables 3 and 4)

TABLE 2. *The effect of sodium nitrate and nitric acid.*

10^2[$NaNO_3$] (M) ...	0	2·5	5[b]	5	10	4	2·5	0
10^2[HNO_3] (M) ...	0	0	0	0	0	1	2·5	5
$10^4 r_0$	5·05	6·17	6·30	6·24	5·80	6·30	5·96	6·05

[Anisic acid] = 0·01M; mean [HOCl] = 0·00487M (range 0·00477—0·00492). *b* denotes that the sodium nitrate was dissolved initially in the anisic acid solution. In the other experiments the strong electrolyte was dissolved in the hypochlorous acid solution.

TABLE 3. *The effect of sodium perchlorate and perchloric acid.*

10^2[$NaClO_4$] (M)	0	2·5	5	10	0
10^2[$HClO_4$] (M)	0	0	0	0	5
$10^6 r_0$	5·05	4·76	5·60	6·56	6·08

[Anisic acid] = 0·01M; mean [HOCl] = 0·00490M (range 0·00487—0·00495).

TABLE 4. *The effect of sodium hydrogen sulphate and sulphuric acid.*

10^2[$NaHSO_4$] (M)	0	2·5	5	10	0
10^2[H_2SO_4] (M)	0	0	0	0	5
$10^6 r_0$	5·15	5·20	5·40	5·95	6·18

[Anisic acid] = 0·01M; mean [HOCl] = 0·00507M (range 0·00505—0·00515).

TABLE 5. *The effect of sodium acetate.*

10^2[NaOAc] (M)	0	5	10
$10^6 r_0$	5·00	4·91	5·15

[Anisic acid] = 0·01M. [HOCl] = 0·00485M.

have little catalytic effect (there are slight signs of inhibition) but higher concentrations increase r_0, the effect of perchlorate being the greater. Sodium acetate has little effect on r_0 (Table 5). The sodium salts thus exert small effects which are generally catalytic and which appear to be roughly in the order of the strengths of the corresponding acids, which is $HClO_4 > HNO_3 > H_2SO_4 \gg$ AcOH. Tables 2 to 4 also show that in the presence of nitric, perchloric, and sulphuric acids r_0 does not differ very greatly from the value with the same concentration of sodium salt. With nitric acid there is no important difference; the effect of 0·05M-perchloric and -sulphuric acids is slightly greater than that of the sodium salts. Now the hydrogen-ion concentration in 75% acetic acid is about 10^{-2}.* Therefore the reaction mixture's being made 0·05M in strong acid will increase the hydrogen-ion concentration approximately five-fold. It thus appears that in 75% acetic acid there is little catalysis by hydrogen ion of the chlorination of anisic acid by hypochlorous acid. Similar results were found in the case of other *p*-alkoxybenzoic acids, and of methyl anisate and *p*-chloroanisole (Part IV). These results are in contrast to those of Branch and Brynmor Jones [3] on the bromination of aromatic ethers by hypobromous acid in 75% acetic acid, and to those on the chlorination of various aromatic compounds by hypochlorous acid in aqueous solution.[1,2] The results in Table 5 on the effect of acetate ions confirm the absence of hydrogen-ion catalysis. Branch and Brynmor Jones found that the bromination was much retarded by sodium acetate's repressing the ionisation of acetic acid.

The Kinetics of the Reaction in 40% *Acetic Acid Solution.*—Table 6 shows that in 40% acetic acid the reaction is of first order in hypochlorous acid up to at least 0·01M. In the notation used for 75% acetic acid, $A = 0{\cdot}095$ and B is certainly less than 5.

Table 7 shows that in 40% acetic acid the catalytic effect of 0·05M-sodium perchlorate is comparable with that found in 75% acetic acid, but there as a much larger effect of perchloric acid. The rate is increased linearly with the concentration of perchloric acid when the perchlorate-ion concentration is maintained constant by addition of sodium perchlorate. The reaction in 40% acetic acid is evidently subject to a considerable catalysis by hydrogen ion. The hydrogen-ion concentration of 40% acetic acid is 0·009; that of 0·05M-perchloric acid in 40% acetic acid will be about 0·052. It can now be seen from

* Values for the hydrogen-ion concentration of concentrated aqueous solutions of acetic acid can be derived from $K_a = 1{\cdot}75 \times 10^{-5}$ at 20° and Kipling's [21] calculations of the amounts of the various molecular species present. The dissociation constant, derived from measurements on dilute solutions, is assumed to refer to the equilibrium between monomeric acetic acid hydrate and the ions, and thus $[H^+] = (K_a[\text{hydrate}])^{\frac{1}{2}}$. The hydrate concentration for aqueous acetic acid of any composition may be calculated from Kipling's graphs.

[21] Kipling, *J.*, 1952, 2858.

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TABLE 6. *The effect of hypochlorous acid concentration in 40% acetic acid.*

10^3[HOCl] (M)	4·27	4·48	5·58	6·70	9·83
$10^4 r_0$	1·18	1·22	1·60	1·92	2·80
$10^4 r_0$/[HOCl]	2·76	2·73	2·87	2·87	2·85

[Anisic acid] = 0·003M.

TABLE 7. *The effect of sodium perchlorate and perchloric acid in 40% acetic acid.*

10^2[$HClO_4$] (M)	10^2[$NaClO_4$] (M)	$10^4 r_0$	$10^4 r_0$ (calc.)
0	0	1·50	—
0	5	1·67	1·67
1·75	3·25	2·60	2·63
3·25	1·75	3·48	3·44
5	0	4·40	4·40

[Anisic acid] = 0·003M; mean [HOCl] = 0·00530M (range 0·00526—0·00533). $10^4 r_0$ (calc.) = $1·67 + 54·5$[$HClO_4$].

Table 7 that raising the hydrogen-ion concentration by about 0·043 increases the rate (at the given concentrations of hypochlorous acid, anisic acid, and perchlorate ion) by 2·73 units. Hence when no perchloric acid is added about 0·57 unit of r_0 is due to a hydrogen-ion catalysed reaction and 1·10 units to an uncatalysed reaction. Comparable figures for 75% acetic acid (estimated from the Figure and Table 3) are about 0·03 and 1·73 respectively.

The Reaction Mechanism.—The virtual absence of any effect of hydrogen ion in 75% acetic acid suggests that it plays no part in the mechanism by controlling the concentration of the chlorinating species. The mechanism involving chlorine cations, found for aqueous solutions by Derbyshire and Waters [1] and by de la Mare, Ketley, and Vernon [2] is thus of little importance in 75% acetic acid. The hypochlorite ion is likewise excluded. For the reasons given earlier, molecular chlorine may also be rejected. Chlorine monoxide, produced by the reversible dehydration of hypochlorous acid, would lead to second-order kinetics in hypochlorous acid.[2] The chlorinating species might be molecular hypochlorous acid in a hydrated state as in aqueous solution but this has generally been found rather unreactive in aromatic substitution,[1,2] although it is effective in addition reactions.[11,12] The remaining possibility is that the observed behaviour of hypochlorous acid is directly connected with the high concentration of acetic acid. There are several observations which are best explained by supposing that there is considerable combination between acetic and hypochlorous acids in 75% acetic acid, and that the chlorinating species arises from this.

When the solvent is changed from 75% to 40% acetic acid there is a great increase in the rate of a hydrogen-ion catalysed reaction. It seems likely that this hydrogen-ion catalysed reaction involves the generation of chlorine cations from molecular hypochlorous acid as in aqueous solution. The suppression of this reaction when the solvent is changed from 40% to 75% acetic acid suggests that the concentration of free molecular hypochlorous acid has been reduced to a very low level in 75% acetic acid. Correspondingly the degree of combination of acetic acid with the hypochlorous acid must rise from a relatively low level in 40% acetic acid to a high value in 75% acetic acid. It is reasonable to attribute the reactivity of hypochlorous acid in 75% acetic acid to this combination of acetic and hypochlorous acids, rather than to residual molecular hypochlorous acid, particularly since the velocity of the reaction that is not catalysed by hydrogen ion rises when the medium is changed from 40% to 75% acetic acid (see above). If a combination of hypochlorous and acetic acids constitutes the chlorinating species in 75% acetic acid, then the factor f of expression (2) should rise greatly when the solvent is changed from 40% to 75% acetic acid. The observed rise in the quantity $B = k_3 f/k_2$ of expressions (1) and (2) is in accord with this, although changes in k_3 and k_2 may also be involved.

Two other observations are in accord with a high degree of combination between acetic acid and hypochlorous acid in 75% acetic acid. First, only a small effect of chloride

ion was observed compared with that found for a reaction in aqueous solution by Derbyshire and Waters,[1] where 10^{-4}M-added chloride increased the rate by 30% (cf. Table 1). This suggests that the formation of chlorine is inhibited. Secondly, the absence from the rate expression of terms of the second order in hypochlorous acid, at concentrations ten times greater than those at which other authors [2,11] have found them to be appreciable, could mean that hypochlorous acid is in a state very different from that in its aqueous solutions.

It seems likely that acetic and hypochlorous acids are mainly combined in the form of a hydrogen-bonded complex, analogous to the acetic acid dimer. There is, however, no obvious reason why such a complex should be any more reactive than hydrated molecular hypochlorous acid, and it is therefore suggested that there is present a small concentration of acetyl hypochlorite which constitutes the chlorinating species: $AcOH + HOCl \rightleftharpoons AcOH,HOCl \rightleftharpoons AcOCl + H_2O$. The presence of acetyl hypochlorite in considerable concentration in solutions containing much water seems unlikely. Acetyl hypochlorite has been prepared in various non-aqueous solvents but has never been isolated.[22] According to Bockemüller and Hoffmann [23] it is readily hydrolysed by water.

The suggestion that acetyl hypochlorite is the chlorinating species brings the present work into agreement with the previous work on hypochlorous acid in sodium acetate–acetic acid buffers. Molecular acetic acid acts as a catalyst for substitution [9] and addition [11,12] reactions of hypochlorous acid in aqueous solutions. The rates of such reactions in buffer solutions rise with increase in acetic acid concentration, while change in the sodium acetate concentration has little effect. This has been taken to mean that acetic acid reacts with hypochlorous acid to give highly reactive acetyl hypochlorite and that the formation and subsequent reaction of the acetyl hypochlorite are not catalysed by hydrogen ion. It should be mentioned, however, that there is disagreement between the properties of the supposed acetyl hypochlorite as observed in the present work and in that with buffer solutions on the one hand, and in the work of de la Mare, Ketley, and Vernon [8] on the other. The latter authors prepared acetyl hypochlorite in glacial acetic acid and found its reactions to be greatly catalysed by hydrogen ion. Further they consider that hypochlorous acid in 98% acetic acid attacks aromatic compounds through intermediate formation of acetyl hypochlorite, the reactions again being catalysed by hydrogen ion. It is possible that the properties of acetyl hypochlorite in this respect vary with the medium and the nature of the organic substrate. It should, however, be borne in mind that the reactive entity in buffer solutions and in 75% acetic acid, which has been presumed to be acetyl hypochlorite, might be merely the hydrogen-bonded complex of acetic and hypochlorous acids postulated above but considered unreactive.

With regard to the nature of the active form of anisic acid there are various possibilities but it is suggested that the most likely are those which connect reaction as an active form with the presence of a high concentration of acetic acid. It may be envisaged that in solution in 75% acetic acid, anisic acid will be combined as complexes both with acetic acid and with water molecules. It is possible that the bulk of the anisic acid is present as hydrated anisic acid and that this is unreactive; the active form would then be a complex of anisic and acetic acids. On the other hand it seems more likely that the bulk of the anisic acid is present as unreactive complex with the acetic acid, while the active form is the hydrated anisic acid molecule.

It is thus suggested that acetic acid is playing a dual rôle in the reaction. On the one hand it serves to produce reactive acetyl hypochlorite from hypochlorous acid; on the other it keeps the bulk of the anisic acid in the form of unreactive complex.

As to the nature of the complexes it seems likely that anisic acid will form hydrogen-bonded complexes with acetic acid and with water analogous to the dimeric form and hydrate of acetic acid itself. This cannot, however, be the only mode of complex

[22] Anbar and Ginsburg, *Chem. Rev.*, 1954, **54**, 925.
[23] Bockemüller and Hoffmann, *Annalen*, 1935, **519**, 174.

formation, for the active and unreactive forms are not restricted to phenolic ethers containing a carboxyl group. Methyl anisate and *p*-chloroanisole show the same kinetic behaviour as anisic acid (Part IV). Hydrogen bonding involving the ether oxygen atom could provide another means of complex formation. There is also the possibility that the complexes are electrostatic in character, since the dipole moments of the aromatic ethers are high. A study of a wide range of compounds at several temperatures in a variety of solvents will be necessary before a final decision can be made as to the nature of the complexes, and indeed before it is certain that the interpretation in terms of complexes is correct.

Salt Effects.—It was shown above that the effects of sodium salts on the initial rate are generally catalytic and in the same order as the strengths of the corresponding acids, *i.e.*, $HClO_4 > HNO_3 > H_2SO_4 \gg AcOH$. de la Mare, Ketley, and Vernon [2] found that the reaction between hypochlorous acid and aromatic compounds in aqueous solution is greatly catalysed by sulphate ions; toluene-*p*-sulphonate ions are rather less effective, and perchlorate ions have scarcely any effect. These observations are explained in terms of the idea that any anion X^-, provided its nucleophilic power is appreciable, will combine with chlorine cations to form a chlorinating species ClX. The large effect of sulphate and the small effect of perchlorate is the opposite of what was found here, and is another indication of the profound difference of mechanism.

The present results resemble more closely those found by Robertson [24] for the halogenation of aromatic compounds by solutions of molecular halogens in acetic acid. In these reactions lithium perchlorate exerts a small catalytic effect, which is roughly the same as that of perchloric acid, while sodium acetate has practically no effect. The effect of chlorides and sulphuric acid is intermediate, and Robertson states that the effects of salts are " in the order of their conductivities ". This is considered to show that the salts exert an activity effect which promotes the anionisation of a halogen atom Ha from the intermediate ArH,Ha_2.

It seems likely that the influence of salts in the present work is explicable along similar lines. Acetyl hypochlorite will probably form a transition complex with the aromatic ether, which will lose first an acetate ion and then a proton to give the chloro-ether. An increase in electrolyte concentration should favour the reaction by promoting the separation of the acetate ion.

Comparison of Reactions of Hypobromous and Hypochlorous Acids in 75% Acetic Acid.—It is interesting that the effective halogenating species for hypochlorous acid should not be analogous to that for hypobromous acid [3] and a tentative explanation can be put forward which may lie in the relative reactivities of the acetyl hypohalites. Acetyl hypochlorite is possibly a much more reactive halogenating species than acetyl hypobromite, just as molecular chlorine is much more reactive than molecular bromine. On the other hand the very reactive halogen cations may well be produced by the reaction with hydrogen ion much more readily for hypobromous acid in 75% acetic acid than for hypochlorous acid in the same medium (Derbyshire and Waters [1] found that in the bromination of sodium toluene-ω-sulphonate in water a second-order velocity constant of 10^{-2} mole $l.^{-1}$ $sec.^{-1}$ could be obtained with $6{\cdot}3 \times 10^{-4}$M-perchloric acid, while a similar velocity in the chlorination required 3·9M-perchloric acid.) Hence it is perhaps not surprising that an acetyl hypohalite mechanism is preferred for hypochlorous acid, while a halogen-cation mechanism predominates for hypobromous acid.

It is further interesting that Branch and Brynmor Jones [3] found no results which suggested the intervention of an active form of ether in the reaction with hypobromous acid in 75% acetic acid. Probably the bromine cations are sufficiently reactive to attack the bulk form of the ether.

The Course of the Reaction.—Although the principal measurements here were of initial

[24] Robertson, *J.*, 1949, 295; 1954, 1267.

rate, some study of the course of the reaction was made. Measurements were carried out up to the point at which about 80% of the hypochlorous acid had reacted. The results are summarised in Table 8. The calculation of $(a - x)$ depends on the assumption that

TABLE 8. *The course of the reaction in 75% acetic acid.*

t (sec.)	$10^3(b - x)$	10^3x	$10^3(a - x)$	t (calc.)
0	6·00	0	10·0	0
89	5·51	0·49	9·51	90
174	5·08	0·92	9·08	176
269	4·63	1·37	8·63	276
537	3·64	2·36	7·64	549
1020	2·45	3·55	6·45	1027
1457	1·75	4·25	5·75	1459
1815	1·34	4·66	5·34	1820

b = initial molar concentration of hypochlorous acid, a = initial molar concentration of anisic acid, x = amount of hypochlorous or anisic acid reacting per litre.

the reaction is not complicated by polysubstitution. On grounds of electronic theory this would not be expected to occur, but the point was checked by measuring the stoicheiometry. When reaction had effectively ceased, 1·03 mol. of hypochlorous acid had reacted with each mol. of anisic acid. The 3% departure from unity is doubtless due to slight autodecomposition of hypochlorous acid.

If the reaction steps over the whole course of the reaction remain as in the mechanism postulated on the basis of initial rate measurements, then

$$dx/dt = A(a - x)(b - x)/[1 + B(b - x)] \quad . \quad . \quad . \quad . \quad . \quad (3)$$

which gives on integration

$$t = \frac{2{\cdot}303}{(a - b)\,A} \log_{10} \frac{b(a - x)}{a(b - x)} - \frac{2{\cdot}303\,B}{A} \log_{10} \frac{a - x}{a} \quad . \quad . \quad . \quad (4)$$

The validity of expression (4) can be tested by using the values of A and B (0·155 and 102 respectively) derived from initial rate studies to calculate times t(calc.) corresponding to the experimental values of x. The values of t(calc.) are in Table 8, and there is good agreement with the experimental values of t. The expression based on initial-rate measurements appears to be valid over at least 80% of the course of the reaction.

In the presence of salts and acids, however, complications may develop during the reaction, for it was found that these influenced the way in which the rate fell. With 0·025M-sodium nitrate the rate falls away rapidly, but at higher concentrations the fall is progressively less marked. Similarly, as sodium nitrate is replaced by nitric acid the fall is less marked. In the case of perchloric and sulphuric acids and their salts such effects seem only slight. Sodium acetate appeared to hold the rate constant over a long period. No explanation of these observations can as yet be offered.

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UNIVERSITY OF HULL. [*Received, August 26th*, 1957.]

52. *Kinetics and Mechanism of Aromatic Halogenation by Hypohalous Acids. Part IV.* Chlorination of Aromatic Ethers by Hypochlorous Acid in 75% Acetic Acid.*

By G. Stanley and J. Shorter.

Reactions of hypochlorous acid in 75% acetic acid with several *p*-alkoxybenzoic acids and with *p*-chloroanisole and methyl anisate have been surveyed. The kinetics and mechanism are similar to those for anisic acid (Part III). The effect of structure upon reactivity is discussed in terms of the constants of the rate equation for *n*-alkyl and *iso*alkyl groups, and for nuclear substituents.

Chlorination of *p*-anisic acid * by hypochlorous acid in 75% acetic acid involves a non-ionic chlorinating species and an active form of *p*-anisic acid. The chlorinating species was tentatively identified as acetyl hypochlorite, and the active form as the hydrated anisic acid molecule, the bulk of the phenolic ether being present as unreactive complex of anisic and acetic acids. We now give a less detailed survey of the reactions of hypochlorous acid with a number of *p*-alkoxybenzoic acids and with *p*-chloroanisole and methyl anisate.

Experimental

The methods used for the purification of acetic acid and for the preparation of hypochlorous acid, and also the technique of initial-rate measurements were described in Part III. Values of r_0 are expressed in moles of HOCl used per litre per second.

The *p*-alkoxybenzoic acids were prepared from *p*-hydroxybenzoic acid by Brynmor Jones's [1] method. The products were recrystallised several times from acetic acid and from benzene to constant m. p.

p-Chloroanisole was prepared from *p*-anisidine by diazotisation and Sandmeyer reaction; it was isolated by steam distillation and purified by repeated distillation under reduced pressure. A commercial sample of methyl anisate was recrystallised several times from ethanol until it gave consistent results in kinetic measurements.

Discussion

Kinetics of the Reaction of Hypochlorous Acid with Aromatic Ethers in 75% Acetic Acid at 20°.—Dependence of initial rate r_0 on ether concentration was examined for four *p*-alkoxybenzoic acids and for *p*-chloroanisole and methyl anisate (Table 1). In all

Table 1. *The dependence of r_0 on ether concentration.*

	(*a*) *p*-Ethoxybenzoic acid			(*b*) *p*-*n*-Propoxybenzoic acid		
10^3[ether] (M)	2·5	4	5	2·5	4	5
$10^4 r_0$	2·36	3·92	4·88	2·55	3·88	4·78
$10^4 r_0$/[ether]	9·44	9·80	9·76	10·2	9·70	9·56
	[HOCl] = 0·00654M.			[HOCl] = 0·00536M.		
	(*c*) *p*-*n*-Butoxybenzoic acid			(*d*) *p*-*iso*Propoxybenzoic acid		
10^3[ether] (M)	2	4		2	3·5	5
$10^4 r_0$	2·18	4·40		3·24	5·64	8·02
$10^4 r_0$/[ether]	10·9	11·0		16·2	16·1	16·0
	[HOCl] = 0·00553M.			[HOCl] = 0·00577M.		
	(*e*) *p*-Chloroanisole			(*f*) Methyl *p*-anisate		
10^3[ether] (M)	5	7	10	5	8	10
$10^4 r_0$	3·50	5·05	7·12	2·03	3·18	4·30
$10^4 r_0$/[ether]	7·00	7·21	7·12	4·06	3·98	4·30
	[HOCl] = 0·00455M.			[HOCl] = 0·005M.		

* Part III, preceding paper.

[1] Brynmor Jones, *J.*, 1935, 1874.

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cases a first-order dependence was found, as for anisic acid. There is no reason to doubt that other *p*-alkoxybenzoic acids would show the same behaviour.

Dependence of rate on hypochlorous acid concentration was examined for eight *p*-alkoxybenzoic acids and for *p*-chloranisole and methyl anisate. The results are shown in Figs. 1—3, those for anisic acid being included for comparison. (To facilitate comparison the results are plotted for an ether concentration of 0·01M. The concentrations used in the actual measurements were as follows: anisic acid and methyl anisate 0·01;

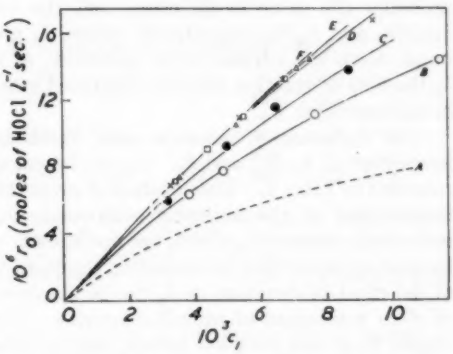
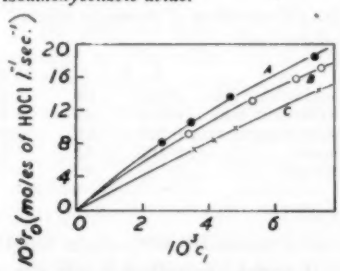


FIG. 1. *The dependence of initial rate r_0 on hypochlorous acid concentration c_1 for* p-n-*alkoxybenzoic acids.*

Ether concentration = 0·01M.

A. Broken line: curve for anisic acid from Part III.
B. ○ p-*Ethoxybenzoic acid.*
C. ● p-n-*Propoxybenzoic acid.*
D. × p-n-*Butoxybenzoic acid.*
E. △ p-n-*Pentyloxybenzoic acid.*
F. □ p-n-*Hexyloxybenzoic acid.*

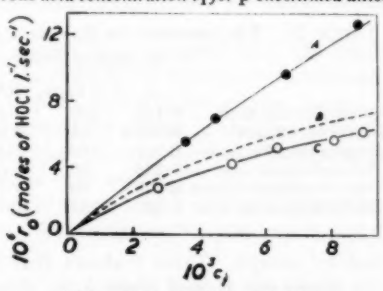
FIG. 2. *The dependence of initial rate r_0 on hypochlorous acid concentration c_1 for* p-iso*alkoxybenzoic acids.*



Ether concentration = 0·01M.

A. ● p-iso*Propoxybenzoic acid.*
B. ○ p-iso*Butoxybenzoic acid.*
C. × p-iso*Pentyloxybenzoic acid.*

FIG. 3. *The dependence of initial rate r_0 on hypochlorous acid concentration c_1 for* p-*substituted anisoles.*



Ether concentration = 0·01M.

A. ● p-*Chloroanisole.*
B. Broken line: curve for anisic acid from Part III.
C. ○ *Methyl anisate.*

p-ethoxy-, *p*-*n*-propoxy-, *p*-*iso*propoxy-, *p*-*iso*butoxy-, and *p*-*iso*pentyloxy-benzoic acids, and *p*-chloroanisole 0·005; *p*-*n*-butoxy-, *p*-*n*-pentyloxy-, and *p*-*n*-hexyloxy-benzoic acids 0·004.) As in the case of anisic acid the relation

$$r_0 = Ac_1c_2/(1 + Bc_1) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

is applicable, where c_1 is the concentration of hypochlorous acid, c_2 is the concentration of ether, and A and B are constants. The values of A and B for each compound are shown in Table 2, and the curves in Figs. 1—3 are drawn with these values of A and B.

The influence of 0·05M-sodium perchlorate, perchloric acid, and sodium acetate was examined for *p*-ethoxy-, *p*-*iso*propoxy-, and *p*-*n*-butoxy-benzoic acids and for *p*-chloroanisole and methyl anisate. The effects of these electrolytes varied somewhat with the ether but not with discernible regularity, so only the overall position is of interest. For

the five compounds, 0·05M-sodium perchlorate increased r_0 on the average by 14% (range 8—19%), and 0·05M-perchloric acid by 16% (range 9—24%); 0·05M-sodium acetate decreased r_0 by 7% (range 4—10%). For anisic acid the effects were in the same direction and the corresponding values were 11, 20, and 2%. Thus in all cases sodium perchlorate and perchloric acid exert small and comparable catalytic effects, and sodium acetate exerts slight inhibition.

The kinetics for higher *p*-alkoxybenzoic acids, and for *p*-chloroanisole and methyl anisate thus closely resemble those for anisic acid. The reaction mechanism is therefore probably the same in all cases, and the constants A and B may be identified with k_1k_3f/k_2 and k_3f/k_2 respectively, where k_1 gives the rate at which unreactive complexes break down to hydrated ether molecules, k_2 the rate of formation of the complexes, and k_3 the rate of reaction between hydrated ether molecules and acetyl hypochlorite present in concentration fc_1.

The Influence of Structure upon Reactivity.—A full discussion of this topic requires knowledge of k_1, k_2, and k_3. k_1 can be calculated as the ratio A/B, and the values are recorded in Table 2. The constant B gives the values of k_3f/k_2, and since f can be assumed independent of the aromatic compound, changes in B reflect changes in k_3/k_2. The individual values of k_3 and k_2 are not known. Suggestions about k_3 can, however, be made by analogy with other halogenation reactions of aromatic ethers, and hence some indication of the effect of structure on k_2 can be obtained. It is also of interest to discuss the values of A as a measure of overall reactivity. The effect of structure will be discussed with regard to *n*- and *iso*-alkyl groups, and nuclear substituents. Since the values of A and, in particular, B are not known with any great precision, discussion can only be general in character.

TABLE 2. *The constants in the rate expression for the chlorination of aromatic ethers by hypochlorous acid in 75% acetic acid.*

	A	$B = k_3f/k_2$	10^3k_1		A	$B = k_3f/k_2$	10^3k_1
p-Methoxybenzoic acid ...	0·155	102	1·52	*p-iso*Propoxybenzoic acid	0·352	48	7·3
p-Ethoxybenzoic acid ...	0·200	51	3·92	*p-iso*Butoxybenzoic acid ...	0·311	45	6·9
p-n-Propoxybenzoic acid	0·217	40	5·43	*p-iso*Pentyloxybenzoic acid	0·215	11	19·6
p-n-Butoxybenzoic acid ...	0·232	29	8·0	*p*-Chloroanisole	0·169	22	7·7
p-n-Pentyloxybenzoic acid	0·223	20	11·2	Methyl *p*-anisate	0·126	91	1·39
p-n-Hexyloxybenzoic acid	0·220	16	13·7				

n-*Alkyl groups.* Table 2 shows that k_1 increases very markedly with chain length. At the same time B, and hence k_3/k_2, decreases. Now it seems likely that k_3 will rise to a maximum at about *n*-butyl, for the reactivity changes in this way in various electrophilic substitution reactions of aromatic ethers. Relative reactivities in halogenation reactions are summarised in Table 3. If k_3 indeed rises with chain length to *n*-butyl, it is evident that k_2 rises even more rapidly. Hence both k_1 and k_2 probably rise with chain length. Until more is known about the active and unreactive forms of the ether it would be premature to attempt to explain the changes in k_1 and k_2 by reference to electronic or steric effects.

The relative values of A can be compared with the relative reactivities in other reactions of aromatic ethers (Table 3). The effect of chain length found in the present work is not so pronounced as that found in the other reactions, but in all cases the effect of alkyl groups of moderate size is almost independent of chain length. There is some indication in the values of A that beyond a certain point the reactivity falls slightly with chain length. Such a fall has been observed with rather longer chains in the other halogenation reactions, particularly in that involving molecular chlorine, where the reactivity is 218 for *n*-heptyl and 201 for *n*-cetyl.

If the effect of structure upon k_3 is comparable with the effect on reactivity in other halogenation reactions, then it would appear that k_1/k_2 decreases somewhat with increase

in chain length, with the result that the effect on A of the change in k_3 is partially compensated.

iso*Alkyl groups.* Table 2 shows that in the series of *iso*alkyl groups k_1 generally increases and k_3/k_2 decreases with chain length, as in the series of *n*-alkyl groups. The small irregularity in the values of k_1 is probably due to the value of B for the *iso*butyl compound being too high. There is no apparent general relationship of the values of k_1 and k_3/k_2 to those of the straight-chain isomers, and the uncertainty in the values makes any detailed discussion unwise.

TABLE 3. *Relative reactivities in the halogenation of aromatic ethers.*

R:	Me	Et	Pr^n	Bu^n	*n*-C_5H_{11}	*n*-C_6H_{13}	Pr^i	Bu^i	*iso*-C_5H_{11}
(*a*) Chlorination by Cl_2 in 99% acetic acid [2]	100	199	223	223	221	221	440	216	—
(*b*) Bromination by HOBr in 75% acetic acid [3]	100	200	225	230	232	—	296 to 396	271	262
(*c*) Chlorination by HOCl in 75% acetic acid	100	129	140	150	144	142	227	201	139

In (*a*) and (*b*) the values given are the mean values of 100 k_{XY}^{OR}/k_{XY}^{OMe}, referring to second-order velocity constants in various series of aromatic ethers 1 : 2 : 4-RO·C_6H_2XY. Except in the case of Pr^i in (*b*) the values vary only slightly with the nature of the nuclear substituents X and Y.
In (*c*) the values given are those of A for the *p*-alkoxybenzoic acids, that for Me being taken as 100.

Table 3 shows that the *iso*propyl group greatly enhances overall reactivity as measured by A. If the effect of this group is compared with that observed in other halogenation reactions, it is seen that in the reactions with molecular chlorine and with hypochlorous acid the ratio Pr^i/Et is greater than Et/Me, but the opposite is found with hypobromous acid.

If the relative values of A for the *iso*alkyl chains are compared with the relative reactivities for the other reactions, it appears quite general for reactivity to increase in the order *iso*-C_5H_{11} < Bu^i < Pr^i. The relationship to the straight chains varies. In the hypobromous acid reaction all the *iso*alkyl compounds are more reactive than their straight-chain isomers; in the reaction with molecular chlorine there is the relationship Bu^n > Bu^i, and in the reaction with hypochlorous acid *n*-C_5H_{11} > *iso*-C_5H_{11}.

Nuclear substituents. When the carboxyl group of anisic acid is replaced by methoxycarbonyl, both k_1 and k_3/k_2 fall slightly (Table 2). When the carboxyl group is replaced by chlorine, k_1 rises greatly and k_3/k_2 falls greatly.

The order of reactivity measured by A is $CO_2Me < CO_2H < Cl$. The effect of the carboxyl group was not studied in the work on hypobromous acid, but the order $CO_2H < CO_2Me < Cl$ was observed in the reaction with molecular chlorine.[4] This sequence can be interpreted in terms of electron-releasing power increasing in the same order. The slightly different order found for the reaction with hypochlorous acid is presumably due to the complexity of the quantity A.

UNIVERSITY OF HULL. [*Received, August 26th*, 1957.]

[2] Brynnmor Jones, *J.*, 1935, 1831.
[3] Branch and Brynmor Jones, *J.*, 1955, 2921.
[4] Bradfield and Brynmor Jones, *J.*, 1928, 1006; 1931, 2903.

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53. *Kinetics of Formation of Ethylenediaminetetra-acetatocobalt*(III) *from the Corresponding Monoaquo- and Monohydroxo-complexes in Aqueous Solutions.*

By I. A. W. Shimi and W. C. E. Higginson.

The kinetics of the formation of CoY^- from $CoYH_2O^-$, $HCoYH_2O$, and $CoYOH^{2-}$ in aqueous solutions have been followed spectrophotometrically (Y^{4-} = ethylenediaminetetra-acetate ion). The reactions of $HCoYH_2O$ and $CoYOH^{2-}$ are thought to be of the S_N1 type, but the unbound carboxylate ion in $CoYH_2O^-$ is believed to displace the ligand water molecule in an S_N2-type reaction.

In addition to the sexidentate complex ion, CoY^-, the ethylenediaminetetra-acetate (enta) anion, Y^{4-}, forms a series of quinquedentate chelate compounds with cobalt(III) in which one of the four carboxylate groups is free.[1,2] The sixth co-ordination position of the cobalt is occupied by a foreign ligand, L, which may be a molecule or a simple anion. Such complexes, represented by $CoYL^{(l-1)+}$, where l is the charge on the foreign ligand, are weak bases, for in solutions of sufficiently low pH the free carboxylate group takes up a proton. The acid dissociation constant of the acid form, $HCoYL^{l+}$, is about 10^{-3} mole $l.^{-1}$ and is little affected by the nature of L. Aqueous solutions of $CoYL^{(l-1)+}$ and $HCoYL^{l+}$ are unstable and eliminate L, forming CoY^-, which shows neither acidic nor basic properties. Aquoethylenediaminetetra-acetatocobalt(III), $CoYH_2O^-$, besides acting as a base, is also an acid of dissociation constant about 10^{-8} mole $l.^{-1}$, the conjugate base being $CoYOH^{2-}$. The pH-dependent relationships between these complexes can be summarised as

$$CoYOH^{2-} \underset{pH>8}{\overset{pH<8}{\rightleftharpoons}} CoYH_2O^- \underset{pH>3}{\overset{pH<3}{\rightleftharpoons}} HCoYH_2O$$

these equilibria being rapidly attained. It is apparent that $CoYOH^{2-}$ and $HCoYH_2O$ cannot coexist in solution in appreciable concentrations. Since in complexes of the type HCoYL the pK of the free carboxylic acid group is about 3, irrespective of the nature of L, it can be concluded that the ratio of the concentrations of the two isomers, $CoYH_2O^-$ and $HCoYOH^-$, is about $10^5 : 1$ at any pH.

The behaviour of certain cobalt(III)–enta complexes as oxidising agents led us to investigate their instability in aqueous solution. Here we present kinetic data on the elimination of the foreign ligand, with consequent formation of CoY^-, from the above three related complexes, obtained by using solutions in water of a solid salt of the anion $CoYOH^{2-}$. Since the species initially present in solution depend upon the pH, which varied in different experiments, we refer for convenience to an aqueous solution of $CoYOH^{2-}$ of any pH in the range studied as a solution of CoY(O), and define $[CoY(O)] = [CoYOH^{2-}] + [CoYH_2O^-] + [HCoYH_2O]$. The elimination reaction was followed spectrophotometrically. Molecular extinction curves of aqueous solutions of the ions CoY^-, $CoYH_2O^-$, and $CoYOH^{2-}$ are shown in Fig. 1; the corresponding curve for $HCoYH_2O$ is very similar to that of $CoYH_2O^-$ at wavelengths greater than 360 mμ and has been omitted for clarity. (These curves duplicate those published previously.[3]) Although in the absence of side-reactions it is possible to determine the individual concentrations of the three CoY(O) species and of CoY^- in solution from measurements of optical density at several different wavelengths, considerable errors are introduced on account of the similarity of the molecular extinction curves. Since the pH-dependent equilibria between the CoY(O) species are rapidly attained and the conversion into CoY^- is quantitative (see Experimental

[1] Schwarzenbach, *Helv. Chim. Acta*, 1949, **32**, 839.
[2] Busch and Bailar, *J. Amer. Chem. Soc.*, 1953, **75**, 4574.
[3] Jørgensen, *Acta Chem. Scand.*, 1955, **9**, 1362.

section), we only needed to estimate [CoY(O)]. Under our conditions, at constant pH, the positive difference $(D_t \sim D_\infty) \propto [CoY(O)]_t$ at any given wavelength, where D_t represents the optical density of the reaction solution in a given cell at time t and D_∞ the optical density in the same cell when the reaction is complete. The precision with which $[CoY(O)]_t$ can be found depends partly upon the magnitude of the change in $(D_t \sim D_\infty)$ for a given change in t, and hence upon the choice of wavelength. Plots of log $[CoY(O)]_t$ against t were linear, so that in most kinetic experiments it was sufficient to plot log $(D_t \sim D_\infty)$ against t, obtaining from the gradient the corresponding first-order velocity constant, $k_{obs} = -\mathrm{d} \ln [CoY(O)]/\mathrm{d}t$.

Fig. 2 shows the variation in k_{obs} with pH at 15° and ionic strength 0·1. If we assume that $HCoYH_2O$, $CoYH_2O^-$, and $CoYOH^{2-}$ each decompose to CoY^-, the corresponding

FIG. 1.

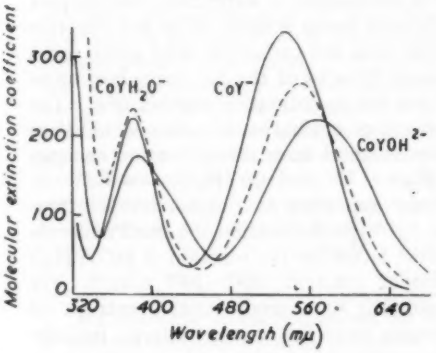
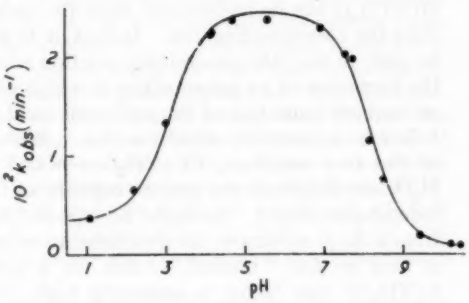


FIG. 2.



first-order velocity constants being k_1, k_2, and k_3, the dependence of k_{obs} upon the hydrogen-ion concentration is

$$k_{obs} = \{k_1[H^+]^2 + k_2K_1[H^+] + k_3K_1K_2\} \div \{[H^+]^2 + K_1[H^+] + K_1K_2\} \quad . \quad (1)$$

where K_1 and K_2 are acid dissociation constants, defined as

$$K_1 = [CoYH_2O^-][H^+]/[HCoYH_2O]; \quad K_2 = [CoYOH^{2-}][H^+]/[CoYH_2O^-].$$

Values found for the velocity constants are given in the annexed Table, $pK_1 = 3{\cdot}1 \pm 0{\cdot}1$, $pK_2 = 8{\cdot}1 \pm 0{\cdot}1$ agreeing with values previously suggested.[1] The theoretical line constructed from these values is shown in Fig. 2. Other experiments at 15° were done at ionic strength 1·0 over the pH range 0·68—6·76, and the values of the constants deduced are $10^2k_1 = 0{\cdot}40 \pm 0{\cdot}05$ min.$^{-1}$, $10^2k_2 = 4{\cdot}6 \pm 0{\cdot}3$ min.$^{-1}$, $pK_1 = 3{\cdot}1 \pm 0{\cdot}2$. These experiments were not extended to alkaline solutions so that the corresponding values of k_3 and pK_2 cannot be given.

By substituting the values of these constants in eqn. (1) it can be seen that at pH = 1, $k_{obs} = k_1$, at pH = 5—6, $k_{obs} = k_2$, and at pH = 10—10·5, $k_{obs} = k_3$. Hence by assuming that changes in the dissociation constants K_1 and K_2 with temperature are small, it was possible to obtain k_1, k_2, and k_3 at ionic strength 0·1 at temperatures other than 15° from kinetic experiments at pH 1·1, 5·6, and 10·5 respectively. From these values, which are summarised in the Table, the following activation energies (ΔE) and temperature-independent factors (A) were obtained: $HCoYH_2O$, $\Delta E_1 = 24{\cdot}9 \pm 1{\cdot}0$ kcal. mole^{-1}, $A = \exp_{10}(16{\cdot}4 \pm 0{\cdot}7)$ min.$^{-1}$; $CoYH_2O^-$, $\Delta E_2 = 25{\cdot}2 \pm 0{\cdot}7$ kcal. mole^{-1}, $A_2 = \exp_{10}(17{\cdot}5 \pm 0{\cdot}5)$ min.$^{-1}$.

Velocity constants (min.$^{-1}$).

Temp.	10^3k_1	10^3k_2	10^3k_3
0°	—	2·21 ± 0·1	—
7·5	0·96 ± 0·05	6·9 ± 0·3	—
15	3·4 ± 0·3	24·4 ± 1·0	0·84 ± 0·04
25	13·3 ± 0·5	—	2·6 ± 0·3

Discussion.—The conformation of enta in its quinquedentate complexes is relatively rigid and the unbound carboxylate group, which is adjacent to the foreign ligand, has little freedom of movement. Consequently a one-stage (S_N2) substitution of the foreign ligand, OH^- or H_2O, by this carboxylate group must be of the vicinal type; an edge-displacement mechanism [4] seems most improbable. The only other simple alternative is an S_N1 substitution in which elimination of the foreign ligand is followed by ring-closure. We suggest that the free carboxylate group in $CoYH_2O^-$ takes part in such an S_N2-type displacement of the ligand, H_2O. The lower rate of elimination of water from the complex $HCoYH_2O$ can be understood, since the carboxylic acid group is likely to be less effective than the corresponding ion. Indeed, it is probable that the carboxylic acid group takes no part in the rate-determining reaction which would thus be of the S_N1 type, leading to the formation of an intermediate in which cobalt has the co-ordination number five. The subsequent ionisation of the carboxylic acid group and co-ordination to cobalt would then follow as a relatively rapid reaction. Within experimental error the activation energies of the two reactions, $HCoYH_2O \longrightarrow CoY^- + H_2O + H^+$ and $CoYH_2O^- \longrightarrow CoY^- + H_2O$, are identical, the greater rapidity of the latter appearing as a higher temperature-independent factor. As might be expected for the S_N1-type elimination of a small molecule from a large substrate, the temperature-independent factor for the reaction of $HCoYH_2O$ is near to the "normal" value for a unimolecular reaction, 10^{15}—10^{16} min.$^{-1}$. For $CoYH_2O^-$ this factor is unusually high, corresponding to a small positive entropy of activation. This is in accord with an S_N2 mechanism, since the negative charge, initially present on the small free carboxylate ion, will be partly transferred to the complex as a whole in the transition state, with consequent liberation of solvated water molecules. We have assumed that $HCoYOH^-$, isomeric with $CoYH_2O^-$, is not of kinetic importance, although the fact that it can only be present in low concentration relative to $CoYH_2O^-$ is no guarantee that this assumption is correct.

The elimination of the hydroxyl ion from $CoYOH^{2-}$ cannot be compared directly with the reactions discussed above since in this complex the oxygen of the expelled ligand is in a different state of combination. However, we should not expect the free carboxylate group to take part in the rate-determining reaction on account of electrostatic repulsion in the transition state between this group and the incipiently-formed hydroxyl ion. Hence we favour the S_N1 mechanism in this case. Reinforcing this suggestion, preliminary experiments on the elimination of bromide ion from the complex ions $CoYBr^{2-}$ and $HCoYBr^-$ showed that the rate of formation of CoY^- is virtually unchanged over the pH range 1—7, the first-order velocity constant being approximately 4×10^{-3} min.$^{-1}$ at 25° and ionic strength 0·1. (These complexes correspond to $CoYH_2O^-$ and $HCoYH_2O$ with Br^- replacing H_2O; pK of the acid $HCoYBr^-$ is [1,5] 3·0.) The obvious interpretation is that in neither bromo-complex does the free carboxylate or carboxylic acid group take part in the rate-determining reaction, and it therefore seems probable that this will be true of the similar complex $CoYOH^{2-}$. If this is so, a low temperature-independent factor is to be expected for the bromo-complexes and $CoYOH^{2-}$ since a unit negative charge, initially spread over the bulk of the complex, excluding the free carboxylate or carboxylic acid group, will be partly concentrated on the bromide or hydroxide ligand in the transition state. The latter is therefore likely to be more strongly solvated than the initial state, with a consequent negative entropy of activation. Although we have not quoted a

[4] Brown, Ingold, and Nyholm, *J.*, 1953, 2674.
[5] Schwarzenbach and Heller, *Helv. Chim. Acta*, 1951, **34**, 576.

temperature-independent factor for the $CoYOH^{2-}$ reaction, a low value, 10^{11}—10^{12} min.$^{-1}$, can be estimated from the values of k_3 in the Table. For the two bromo-complexes the corresponding value is $10^{12.7}$ min.$^{-1}$, again low for a unimolecular reaction.

Experimental

Reagents were "AnalaR" or were purified by appropriate methods. Sodium ethylenediaminetetra-acetatocobalt(III) tetrahydrate was prepared *via* sodium hydrogen bromoethylenediaminetetra-acetatocobalt(III) trihydrate as previously described.[1] Dihydrogen aquoethylenediaminetetra-acetatocobalt(II) dihydrate was prepared by mixing equal volumes of 0·5M-cobalt sulphate and 0·5M-disodium dihydrogen ethylenediaminotetra-acetate dihydrate and concentrating the solution to half its original volume. After 1 day, crystals of the *complex* were obtained [Found: Co, 14·3%; *M*, 408 (pH titration). $H_2Co(C_{10}H_{12}O_8N_2),3H_2O$ requires Co, 14·6%; *M*, 403·2]. 20 g. of this complex were dissolved in about 60 ml. of *ca.* M-sodium carbonate solution, the final pH being about 9. The solution was cooled to 0°, and maintained at 0° for the remainder of the preparation. 25 ml. of cold hydrogen peroxide (100-vol.) were added gradually with stirring. At the end of the addition the pH was adjusted, if necessary, to 9. When evolution of oxygen ceased, 200 ml. of ethanol, cooled to 0°, were added with stirring. A dark-blue oily liquid separated and the supernatant aqueous ethanol was then decanted. A small quantity of cold absolute ethanol was added with vigorous stirring, decanted, and the process repeated until the oil solidified. After further washing and decantation the blue solid was filtered off and dried under vacuum at room temperature over anhydrous magnesium perchlorate. The solid, a hydrate of disodium hydroxoethylenediaminetetra-acetatocobalt(III), is hygroscopic, and unstable when moist [Found: C, 26·0; H, 3·80; Co, 12·1%; *M*, 476 (pH titration). Calc. for a trihydrate: $Na_2Co(C_{10}H_{12}O_8N_2)OH,3H_2O$: C, 25·9; H, 4·12; Co, 12·7%; *M*, 464]. Samples of the complex gave quantitative decomposition in acetate buffers to CoY^- within 3% as shown spectrophotometrically.

The molecular extinction curves for CoY^- and the three CoY(O) species were determined in buffered solutions by using a Unicam S.P. 500 spectrophotometer. The pH values of the solutions were 1·1 for $HCoYH_2O$, 5·6 for $CoYH_2O^-$ and CoY^-, and 10·5 for $CoYOH^{2-}$. On account of their instability, solutions of the CoY(O) complexes were frequently renewed. Solutions of the four complexes, and appropriate mixtures, obeyed Beer's law at the wavelengths used in the kinetic experiments.

Solutions for kinetic experiments were made by dissolving a known weight of the solid hydroxo-complex in various aqueous buffer solutions; the ionic strength was made 0·1 or 1·0 by the addition of potassium chloride solution. In most experiments the concentration of the cobalt complex was 2—4 $\times$ 10^{-3}M. The buffers and corresponding pH ranges were phosphoric acid–dihydrogen phosphate (2—3), acetic acid–acetate (4—5·6), dihydrogen phosphate–monohydrogen phosphate (6—7·5), boric acid–borate (8—9·4) and bicarbonate–carbonate (10—10·5). Hydrochloric acid was used for experiments at pH = 0·7—1·6. The pH of the solution was measured (by meter) at the beginning and end of each kinetic experiment. Reactions were carried out in stoppered flasks in a thermostat, and samples were removed at intervals for measurement of the optical density at various wavelengths. Measurements were made at 500 and 576 mμ. Readings at 500 mμ were used to construct the logarithmic plots against time. At 576 mμ the molecular extinction coefficients of the three CoY(O) species and CoY^- are almost identical and the constancy of these measurements showed the absence of side-reactions from pH 0·7 to 7·0. From pH 7·0 to 10·5 measurements were also taken at 349 and 620 mμ and it was possible to calculate the separate concentrations of CoY^-, $CoYOH^{2-}$, and $CoYH_2O^-$. Although these were subject to considerable error and were unsatisfactory for kinetic plots, it was evident that the ratio $[CoYOH^{2-}]/[CoYH_2O^-]$ remained approximately constant throughout the reaction. In these experiments in alkaline solutions, the optical density at 576 mμ decreased slightly with time, showing the presence of a side-reaction which we believe results in the formation of CoY^{2-}, the enta complex of cobalt(II). The extent of this side-reaction was never more than 5% of the total. At pH values in excess of 10·5 the extent of the side-reaction was increased.

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54. *The Relative Affinities of Co-ordinating Atoms for Silver Ion. Part I. Oxygen, Sulphur, and Selenium.*

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Water-soluble sulphonated aromatic ethers, sulphides, and selenides were prepared and the stability constants of their complexes with silver ion determined. These are listed in Table 1. The ether oxygen has little if any tendency to co-ordinate, but the sulphides and selenides form complexes of moderate stability up to $\bar{n} = 4$ without the stop, usually considered characteristic of silver complexes, at $\bar{n} = 2$. The replacement of the bivalent sulphur atom by selenium in *p*-$SPh{\cdot}C_6H_4{\cdot}SO_3Na$ increases the first stability constant from 47 to 430 l. mole^{-1}, equivalent to about 1·3 kcal. mole^{-1} in $\Delta G°$. The replacement of the phenyl group by an ethyl group similarly increases the stability constant.

THERE is little quantitative information on the relative tendencies of molecules containing donor atoms from Groups V and VI of the Periodic Table, other than nitrogen and oxygen, to form complexes with acceptor molecules and ions. This, and the qualitatively observed stabilities of complex compounds, together with extensive quantitative data on the stabilities of halide complexes, indicate that acceptor atoms are of two general types: (*a*) those which form their most stable complexes with the first atoms of each Group of donor atoms in the Periodic Table (*viz.* N, O, and F); and (*b*) those which form their most stable complexes with the second (*viz.* P, S, and Cl) or a subsequent donor atom of each Group. In this context each oxidation state of a metal atom must be regarded as a different acceptor atom, *e.g.*, Co^{2+} is a different acceptor atom from Co^{3+}.

The few quantitative data about complex formation by the heavier donor atoms have been obtained mainly from vapour-phase equilibria and concern solely atoms of class (*a*), *e.g.*, Al, or of only very weak class (*b*) character,[1] *e.g.*, B in BH_3. Our present objects are (i) to measure quantitatively the tendencies of ligands containing donor atoms from Groups V and VI, other than nitrogen and oxygen, to form complexes with metal ions in class (*b*); and (ii) to obtain information on the relative double-bonding tendencies of the heavier donor atoms, since class (*b*) character appears to be associated with d_π or dative π-bonding between the metal and ligand.

Most of the metals of class (*b*) form inert non-volatile complexes which, in general, cannot be examined by equilibrium methods. Of those which form labile complexes, silver(I) appears to be the most promising for study, and it is preferable to examine its tendency to form complexes in aqueous solution because most existing stability-constant data relate to that medium.

Our knowledge of the formation of complexes in aqueous solution is based largely on measurements involving halide ions and ligands in which nitrogen and oxygen are the donor atoms. The pioneer work in this field by J. Bjerrum,[2] Leden,[3] Schwarzenbach,[4] Calvin,[5] and their co-workers has been followed by a flood of such data. The extension of their methods to organic ligands containing the heavier donor atoms of Groups V and VI has been slow because such ligands are often spontaneously oxidised by air and are insoluble in water; their complexes are also insoluble. Recently, by methods similar to those used by J. Bjerrum, some quantitative data regarding the co-ordination of sulphur

[1] See Graham and Stone, *J. Inorg. Nuclear Chem.*, 1956, **3**, 164, and references therein.
[2] J. Bjerrum, "Metal Ammine Formation in Aqueous Solution," Haase and Son, Copenhagen, 1941.
[3] Leden, *Z. phys. Chem.*, 1941, *A*, **188**, 160.
[4] Schwarzenbach, Kampitsch, and Steiner, *Helv. Chim. Acta*, 1945, **28**, 828, 1133.
[5] Calvin and Wilson, *J. Amer. Chem. Soc.*, 1945, **67**, 2003.

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ligands with a few metal aquo-ions have been obtained by employing chelating sulphido- and mercapto-amines and acids.[6, 7, 8] The use of chelating ligands with Ag^I is not desirable because they cannot accommodate themselves to the linear co-ordination which occurs in the usual 2-co-ordinated silver complexes but give rise to polynuclear complexes.[9] Unidentate ligands are thus essential; to obtain sufficient resistance to oxidation we chose phenyl derivatives, and their insolubility in water was overcome, but only just, by the introduction of one or more sulphonic acid groups. We now record observations on the formation of silver complexes by the sulphonated ether, organic sulphides, and the selenide listed in Table 1.

These sulphonated ligands each contain three different types of co-ordinating groups: (i) the ether oxygen and bivalent sulphur and selenium atoms respectively, (ii) the benzene nucleus, and (iii) the sulphonate ion group. To determine whether the last two were of any consequence, the formation of silver ion complexes by sodium benzenesulphonate was examined. Its co-ordinating capacity was negligible compared with that of the sulphonated sulphides and selenide, and so we may safely assume that complex formation takes place through their bivalent sulphur and selenium atoms. The formation of silver complexes by the sulphonated ether was of the same low order as that by sodium benzenesulphonate, and so the co-ordinating atom or group in the ether has not been established.

The formation of labile complexes by a ligand, L, and hydrated metal ion, M, in aqueous solution occurs through a series of rapidly established equilibria which may be defined by the equilibrium or stability constants, K_1, K_2, etc., or β_1, β_2, etc., as follows. The charges associated with the ions and metal ion have been omitted for clarity.

$$\begin{array}{llll} M + L \rightleftharpoons ML; & K_1 = [ML]/[M][L]; & \beta_1 = K_1 & \\ ML + L \rightleftharpoons ML_2; & K_2 = [ML_2]/[ML][L]; & \beta_2 = [ML_2]/[M][L]^2 & = K_1K_2 \\ \text{etc. to} & \text{etc. to} & \text{etc. to} & \\ ML_{N-1} + L \rightleftharpoons ML_N; & K_N = [ML_N]/[ML_{N-1}][L]; & \beta_N = [ML_N]/[M][L]^N & = K_1K_2 \ldots K_N \end{array}$$

The K's are known as " stepwise " or " consecutive " stability constants and the β's as " gross " or " cumulative " stability constants. The stability constants β_1, β_2, etc., were determined at 25° by potentiometric titration of silver perchlorate with the sodium salts of the ligands, L, by use of Ag,AgCl or Ag,AgBr electrodes to determine the free $[Ag^+]$ in solution.

To keep activity coefficients as constant as possible the solutions were adjusted with sodium perchlorate to the same initial ionic strength, I. In the case of the sulphonated sulphides and selenide the ionic strength was limited by the solubilities of the salts involved, and rather low ionic strengths of 0·1 and 0·2M were used. The limit in the case of the *p*-ethylthiobenzenesulphonate ion was set by the rather poor solubility of the sodium salt in sodium perchlorate solutions of more than 0·2M, and in the case of the *p*-ethylselenobenzenesulphonate ion by that of the silver salt. Nevertheless, both ligands form complexes sufficiently strongly for the main part of complex formation to take place within the limited available range of concentrations, [L], of the free ligands. For comparison the two sulphonated diphenyl sulphides were investigated at the same ionic strength. The more strongly co-ordinating monosulphonate gave a sufficient range of concentration to cover most of the complex-formation function, but the values of K_n/K_{n+1} are so small that the second and third complexes ($n = 2$ and $n = 3$) have only a very short range of existence (Fig. 1), and so are always in equilibrium with relatively large quantities of the first and fourth complexes. This means that K_2 and K_3 cannot be accurately determined. Using the more weakly co-ordinating disulphonate we could cover only the first part of the formation function. Even so, valuable conclusions may be drawn. K_1, which is the

[6] Gonick, Fernelius, and Douglas, *J. Amer. Chem. Soc.*, 1954, **76**, 4671.
[7] Fielder, Rescigno, and Radicca, *Gazzetta*, 1955, **85**, 453.
[8] Ågren and Schwarzenbach, *Helv. Chim. Acta*, 1955, **38**, 1920.
[9] Schwarzenbach, Ackermann, Maissen, and Anderegg, *Helv. Chim. Acta*, 1952, **35**, 2337.

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most accurately determined constant, is also the most reliable constant from which to determine the relative affinities of the various heavy donor atoms for Ag^+, since steric and other extraneous factors are least important when the addition of the first molecule of ligand to the hydrated metal ion takes place. For the very weakly co-ordinating benzenesulphonate and *p*-methoxybenzenesulphonate ions the range of concentration of the free ligand, [L], had to be extended considerably, and fortunately solubility relationships allowed this. A higher ionic strength was thus necessary and 1·0M was used for these two ligands.

The stability constants, K, for the various ligands, L, were calculated by Leden's [3] method as developed by Fronaeus [10] (Table 1): $\log K_1$, also listed, gives a relative measure of the affinities of the various ligands for silver ion.

TABLE 1. *Concentration stability constants, K (l. mole^{-1}), of the ligands, L, with silver ion at an ionic strength I* (M) *and* 25°.

Ligand "L"	I	K_1	K_2	K_3	K_4	$\log K_1$
$PhSO_3^-$ *	1·0	0·9	—	—	—	−0·04
p-MeO·C_6H_4·SO_3^- *	1·0	0·76	0·8	—	—	−0·12
p-Et**S**·C_6H_4·SO_3^- †	0·1	415	48	~25	—	2·62
	0·2	390	49	17	11	2·59
p-Ph**S**·C_6H_4·SO_3^- †	0·1	47	22	13	40	1·67
	0·2	47	12	16	85	1·67
S(C_6H_4·SO_3^--*p*)$_2$ †	0·2	25	8	~45	—	1·40
p-Ph**Se**·C_6H_4·SO_3^- †	0·1	430	180	35	170	2·63

* The donor atoms which take part in complex formation are not known with certainty, but are probably oxygen atoms of the SO_3^- group.

† The donor atoms taking part in complex formation are those in heavy type.

Several interesting points emerge from the constants listed. (1) The class (*b*) character of silver, well known from its general complex chemistry, is apparent. The ether oxygen atom is attached only very weakly, if at all, to silver ion in dilute aqueous solution, whereas the sulphides and selenides give much more stable complexes.

(2) In comparison with the common ligands which give very stable silver complexes, the sulphides and selenides listed in Table 1 give complexes of only moderate stability. The K_1's ranging from 25 to 430 l. mole^{-1} indicate that the complexes have a stability of the same order as the silver–pyridine complex [11] (K_1 = 110 l. mole^{-1}), and are much weaker than those of primary aliphatic amines,[11] ammonia,[12] and the halide ions: [13,14,15] for L = NH_2Et, K_1 = 2340; for L = NH_3, K_1 = 1740; for L = Cl^-, K_1 = 700; for L = Br^-, K_1 = 14,000; and for L = I^-, $K_1 = 1{\cdot}3 \times 10^8$ l. mole^{-1}. In making these rough comparisons no allowance was made for the differences in ionic strength at which the constants were measured, or for slight differences in temperature.

(3) Silver(I) ion is usually considered to have a characteristic co-ordination number of 2, although 3 is not unknown [16] and 4 occurs in some of its solid complexes [17] and in halide [13,14,15] and cyanide [18] solutions. Usually, where successive stability constants have been determined, it is found that the first two monodentate ligands are attached strongly to the silver ion, and in those few cases where further ligand molecules are taken up by the ion they are comparatively weakly held, *i.e.*, there is a definite "stop" in complex formation after two ligand molecules have been taken up. We shall discuss this subject in the light of further examples in a later paper, but here merely note the absence

[10] Fronaeus, "Komplexsystem hos Koppar," Gleerupska Univ.-Bokhandeln, Lund, 1948, p. 18 *et seq.*
[11] Bruehlman and Verhoek, *J. Amer. Chem. Soc.*, 1948, **70**, 1401.
[12] Ref. 2, p. 130.
[13] Berne and Leden, *Svensk kem. Tidskr.*, 1953, **65**, 88.
[14] Berne and Leden, *Z. Naturforsch.*, 1953, **8***a*, 719.
[15] Leden, *Acta Chem. Scand.*, 1956, **10**, 535.
[16] See Cass, Coates, and Hayter, *J.*, 1955, 4007.
[17] Mann, Wells, and Purdie, *J.*, 1937, 1828.
[18] Jones and Penneman, *J. Chem. Phys.*, 1954, **22**, 965.

of any major stop in the formation of silver complexes by the sulphide and selenide ligands until four ligand molecules have been accommodated, and the very short range of existence of the second complexes ($n = 2$) (see Fig. 1). This agrees with Lindqvist and Strandberg's [19] observation that silver appears to be reluctant to form linear complexes containing sulphur as ligand atoms. In this respect selenium evidently resembles sulphur. With sodium *p*-ethylthiobenzenesulphonate there is a very slight retardation after the addition of the first ligand, but generally all the ligand molecules are taken up uniformly. In the case of the dianion of di-(*p*-sulphophenyl) sulphide (p-$^-O_3S{\cdot}C_6H_4{\cdot}S{\cdot}C_6H_4{\cdot}SO_3^-$-$p$), where only three complexes can be proved in the range of concentration of L which we investigated, addition of the fourth ligand molecule might be delayed. To determine

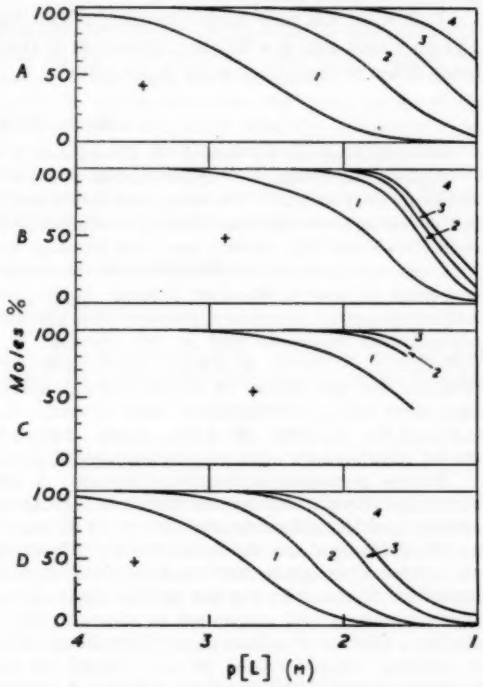
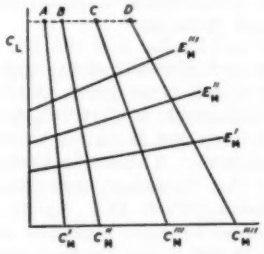


FIG. 1. *Regions of stability of the complex ions* AgL_n *showing the percentages of the total silver content in the form of the various complexes and their variation with* [L] *at* 25°.

A, L = *p*-EtS·C_6H_4·SO_3^-, $I = 0{\cdot}2$.
B, L = *p*-PhS·C_6H_4·SO_3^-, $I = 0{\cdot}1$.
C, L = p-$^-O_3S{\cdot}C_6H_4{\cdot}S{\cdot}C_6H_4{\cdot}SO_3^-$-$p$, $I = 0{\cdot}2$.
D, L = *p*-PhSe·C_6H_4·SO_3^-, $I = 0{\cdot}1$.

The regions labelled +, 1, 2, 3, 4 refer to those occupied by Ag^+, AgL_1, AgL_2, AgL_3, AgL_4 respectively.

FIG. 2.



whether this is so would require the investigation of higher values of ligand concentration and a higher ionic strength, but solubility relationships do not allow this.

(4) Qualitatively, Coates [20] has shown that the stabilities of complexes formed by organic sulphides, selenides, and tellurides with silver iodide increase in that order. Our quantitative measurements confirm this order for sulphide and selenide complexes, and show that the difference in stability is represented in our complexes by a factor of 9 in the first stability constants, K_1, equivalent to about 1·3 kcal. mole^{-1} in $\Delta G°$. This order of stabilities may be contrasted with that qualitatively observed in the platinous chloride series, where dialkyl sulphide complexes are undoubtedly very much more stable than the corresponding selenide complexes.[21]

(5) It is generally observed qualitatively that aliphatic derivatives of the heavier donor atoms form more stable complexes than the aromatic. We have confirmed this and

[19] Lindqvist and Strandberg, *Acta Cryst.*, 1957, **10**, 173.
[20] Coates, *J.*, 1951, 2003.
[21] Chatt and Venanzi, *J.*, 1955, 2787.

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obtained a quantitative measure of the difference. The replacement of the phenyl group by an ethyl group in *p*-ethylthiobenzenesulphonic acid increases the stability constant by a factor of about 9, *i.e.*, about 1·3 kcal. mole^{-1} in $\Delta G°$.

Generally it can be seen from Fig. 1 that the formation of silver complexes in aqueous solution by organic sulphides and selenides contrasts markedly with their formation by ammonia and primary amines. The important difference is the absence of a "stop" in complex formation at $\bar{n} = 2$. This "stop" has hitherto been considered to be characteristic of the formation of silver(I) and related complexes [*e.g.*, mercury(II)]. In most respects the silver ammines appear to represent one extreme type of silver complex and the sulphide and selenide complexes another, with the chloride and bromide ion complexes truly intermediate between these two types.

This work has now been extended to the sulphonated aromatic amines, a phosphine, and an arsine and so a detailed discussion of the shapes of the complex-formation curves is being deferred until that work is described.

Experimental

Microanalyses are by Messrs. W. Brown and A. G. Olney of these laboratories.

Sodium Sulphonates.—Prepared as below and dried, their purity was established by analyses and equivalent weight. The latter was determined by running a known quantity of the sodium salt in hot aqueous solution through a column containing the acid form of a cation-exchange resin (Zeo-Karb 225), eluting, and then titrating the liberated acid.

Commercial sodium benzenesulphonate was twice recrystallised from 70% aqueous methanol and dried *in vacuo* at 80—100° (Found: equiv., 180·2. Calc. for $C_6H_5O_3SNa$: equiv., 180·2). Sodium *p*-methoxybenzenesulphonate was prepared by direct sulphonation of anisole with concentrated sulphuric acid at 90° (Found: C, 39·8; H, 3·4%; equiv., 210. Calc. for $C_7H_7O_4SNa$: C, 40·0; H, 3·4%; equiv., 210). Sodium *p*-ethylthiobenzenesulphonate [22] was prepared by the action of sodium ethyl sulphide on an alcoholic suspension of the solid diazonium salt of *p*-sulphanilic acid (Found: C, 39·8; H, 4·0%; equiv., 241. Calc. for $C_8H_9O_3S_2Na$: C, 40·0; H, 3·8%; equiv., 240). Sodium *p*-phenylthiobenzenesulphonate and the *pp'*-disulphonate were prepared as described by Chatt and Williams.[23]

Sodium p-*phenylselenobenzenesulphonate.* A solution of sulphanilic acid (35 g.), sodium hydroxide (8·8 g.), and sodium nitrite (8·5 g.) in water (320 c.c.) at 0° was slowly added with stirring to dilute sulphuric acid (50 c.c. of concentrated acid in 600 c.c. of water) with cooling, so that the temperature did not exceed 3°. The explosive diazonium salt, $N_2{\cdot}C_6H_4{\cdot}SO_3$, separated as a granular precipitate and was filtered off, washed with ice-water and drained in the Buchner funnel for 30 min. It was not pressed down during this operation. The solid was then very gently removed and suspended in ethanol (100 c.c.). To this suspension was added with stirring a solution of sodium phenyl selenide and free selenophenol (PhSeH, 21 g.; NaOH, 3·75 g.) in aqueous ethanol (water 30 c.c.; EtOH, 85 c.c.). Vigorous nitrogen evolution occurred throughout the addition and when this had subsided concentrated aqueous sodium hydroxide was slowly added until the solution was permanently red. The solution was now warmed (water bath) until it became clear (5 min.) and then kept in a freezing mixture. The *product* separated as a yellow solid, which was filtered off, washed with alcohol, then ether, and dried (24 g.). It was twice recrystallised from aqueous ethanol and so obtained as a pale cream solid (6 g.) (Found: C, 42·6; H, 3·0%; equiv., 335·0. $C_{12}H_9O_3SNaSe$ requires C, 43·0; H, 2·7%; equiv., 335·2). The *benzylisothiuronium* salt, recrystallised from aqueous ethanol, had m. p. 154—155° (Found: C, 50·3; H, 4·3; N, 6·1. $C_{20}H_{20}O_3N_2S_2Se$ requires C, 50·1; H, 4·2; N, 5·85%).

Determination of the Stability Constants.—Leden's method [3] as modified by Fronaeus [10] was used, and since the modification used has appeared only in Swedish we summarise the relevant part in an Appendix, where terms not defined below are also given.

Experimental Technique.—Silver perchlorate solution of a concentration C_M' in the right-hand half-cell (Appendix) was titrated with ligand solution of a concentration C_L'. The free silver-ion concentration [Ag^+] (= M) was measured by means of silver halide electrodes, as pure

[22] Stadler, *Ber.*, 1884, **17**, 2077.
[23] Chatt and A. A. Williams, *J.*, 1956, 3246.

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silver electrodes are unsatisfactory.[24] Both chloride and bromide electrodes were used. They were prepared according to Brown,[25] from wire of 1 mm. diameter and about 2 cm. long. Both kinds of electrode gave the same potentials when immersed in the same solution, and from the initial potentials E_0 measured in solutions of known $[Ag^+]$ $(= C_M)$ they were shown to obey Nernst's law.

The bromide electrodes were the more useful because they could be used in solutions of much lower $[Ag^+]$ without being perceptibly dissolved. In fact, the chloride electrodes were markedly dissolved at the highest concentration of *p*-phenylselenobenzenesulphonate used, but the bromide electrodes were satisfactory throughout the whole investigation.

Both kinds of electrode gave much the same reproducibility, as a rule 0·1 mv at low values, and 0·3—0·4 mv at higher values of E_M. Every solution was measured with two electrodes, and every titration series repeated at least once. The mixing of the solutions during the titrations was brought about by a stream of pre-saturated nitrogen free from oxygen.

The reference electrode was a gold–quinhydrone electrode in 0·01M-perchloric acid containing sodium perchlorate to the same ionic strength as the other half-cell. The bridge joining the half-cells contained sodium perchlorate solution of the same ionic strength.

At every point during the titrations C_M and C_L were known from the compositions of the solutions used. As the ligand solution did not contain any silver ions, C_M continuously decreased as C_L increased. The difference between the e.m.f. E at a definite point in the titration, and the initial e.m.f., E_0', due to the reduction of the silver-ion concentration, was therefore caused by dilution as well as by the formation of complexes. To find the difference E_M defined in eqn. (7) (Appendix) as due only to the formation of complexes, a correction was necessary, as follows:

The initial e.m.f. E_0' is given by equation (i) [cf. (6); Appendix]:

$$E_0' = E_k + (\boldsymbol{RT}/\boldsymbol{F}) \ln C_M' \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad \text{(i)}$$

If the electrode vessel initially contained "*a*" c.c. of silver solution (concentration C_M') and "*v*" c.c. of the ligand solution were then added, the total silver concentration would decrease to $C_M = C_M' \cdot a/(a + v)$. Hence

$$E_0' = E_k + (\boldsymbol{RT}/\boldsymbol{F}) \ln C_M + (\boldsymbol{RT}/\boldsymbol{F}) \ln [(a + v)/a] = E_0 + (\boldsymbol{RT}/\boldsymbol{F}) \ln [(a + v)/a]$$

and

$$E_M = E_0 - E = E_0' - E - (\boldsymbol{RT}/\boldsymbol{F}) \ln [(a + v)/a] \quad . \quad . \quad . \quad . \quad \text{(ii)}$$

At least three different silver concentrations, C_M', were titrated, except when the ligand had little affinity for the metal ion; in this case $C_L \approx [L]$, and only two concentrations were needed.

When E_M is plotted against C_L a family of curves is obtained similar to those of Fig. 3 (Appendix), but with the total silver concentration C_M decreasing along each curve. By combining $C_M = C_M' \cdot a/(a + v)$ and $C_L = C_L' \cdot v/(a + v)$ the following linear connection between C_M and C_L is found:

$$C_M = C_M' - (C_M'/C_L')C_L \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad \text{(iii)}$$

In obtaining a plot of C_M against C_L at constant E_M [cf. Fig. 4 (Appendix)) either this formula could be used, or, more simply, C_M' plotted against C_L by using a contracting abscissa as in Fig. 2. This is most readily constructed by plotting the points *A*, *B*, etc. corresponding to $v = a$, where $C_L = \frac{1}{2}C_L'$ and $C_M = \frac{1}{2}C_M''$, etc., then joining the appropriate points *A* to C_M', *B* to C_M'' etc. The required C_M points lie along those lines at the known values of C_L. The points of constant E_M are then joined and the lines extrapolated to cut the C_L axis to give [L] as described in the Appendix.

Systems Investigated.—The experimental results are recorded in the Tables. Concentrations are millimolar (mM) and e.m.f.'s in mv. The temperature was 25° c. Other terms are as follows: C_L, total concentration of ligand in the right-hand half-cell; C_L', concentration of the ligand solution added; C_M', concentration of silver ion in the right-hand half-cell before the addition of ligand solution; E_M, difference between the e.m.f. of the cell containing the ligand C_L, and its e.m.f. had no ligand been present [eqns. (7, Appendix) and (ii)]; β and K, stability constants defined on p. 265; [L], concentration of free ligand; and X, X_1, etc., functions defined as in eqns. (3), (4), and (7) (Appendix).

[24] Leden, *Svensk kem. Tidskr.*, 1946, **58**, 129.
[25] Brown, *J. Amer. Chem. Soc.*, 1934, **56**, 646.

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Sodium benzenesulphonate has a very weak affinity for silver ion and so the measurements had to be made at high ligand concentrations, necessitating a high ionic strength. In these circumstances, at moderate concentrations of silver ion (<20 mM) $[L] \approx C_L$ and is thus independent of C_M. Since E_M is a function of [L] only [eqns. (3) and (7)], E_M should also be independent of C_M, unless polynuclear complexes are formed. Polynuclear complexes would be formed if both the sulphonic acid group and the benzene nucleus took up silver ion. In fact, E_M was independent of C_M and the experimental values are recorded in Table 2. X_1 is constant, indicating that complex formation does not proceed beyond the first complex over the range of C_L studied.

Sodium *p*-methoxybenzenesulphonate has a weak affinity for silver ion and a high ionic strength was necessary as with the benzenesulphonate. E_M was not quite independent of C_M and the constants were calculated in the normal manner from three values of C_M' (Table 3).

TABLE 2. *The system silver ion–benzenesulphonate ion* ($C_L' = 1$M; $I = 1$M).

$C_L = [L]$	13·17	38·5	62·6	117·8	116·7	210·5	250
E_M	0·3	0·8	1·3	2·5	3·5	4·4	5·3
X	1·012	1·032	1·052	1·102	1·146	1·186	1·229
X_1	0·91	0·83	0·83	0·86	0·87	0·88	0·92

$\beta_1 = K_1 = 0{\cdot}9 \pm 0{\cdot}1$ l. mole^{-1}.

Sodium *p*-ethylthiobenzenesulphonate was too insoluble in sodium perchlorate solutions to be used at ionic strengths greater than about 0·2M. The first determinations were made at an ionic strength of 0·1M (Table 4), but a sufficient range of ligand concentrations to determine all the constants could not be covered at this low ionic strength and a further determination at an ionic strength of 0·2M was made (Table 5). No crystalline precipitate was obtained during any of these experiments, but a slight cloudiness developed at high ligand concentrations.

Sodium and silver *p*-phenylthiobenzenesulphonates were so slightly soluble in 0·1M-sodium perchlorate that measurements were limited to solutions of low silver ($C_M' = 5$ mM) and ligand concentrations. At higher silver concentrations the *silver salt* was precipitated (Found: C, 38·6; H, 2·45; Ag, 28·7. $C_{12}H_9O_3S_2Ag$ requires C, 38·6; H, 2·4; Ag, 28·9%). In spite of the short range of concentrations available most of the complex-formation curve was covered during the

TABLE 3. *The system silver ion–*p*-methoxybenzenesulphonate ion* ($C_L' = 1$M; $I = 1$M).

A. E_M as a function of C_L.

$C_M' \longrightarrow$ 20	10	5	$C_M' \longrightarrow$ 20	10	5	$C_M' \longrightarrow$ 20	10	5
C_L	E_M	E_M	E_M	C_L	E_M	E_M	E_M	C_L	E_M	E_M	E_M
13·2	0·6	0·6	0·6	116·7	7·9	7·9	8·0	348	17·9	18·1	18·4
38·5	1·7	1·7	1·8	210·5	10·2	10·2	10·3	400	21·2	21·4	21·9
62·5	2·9	2·8	2·9	250	12·3	12·4	12·6	444	24·1	24·4	25·0
90·9	4·2	4·2	4·3	285	14·3	14·4	14·7	500	28·0	28·4	29·1
117·6	5·5	5·4	5·6	318	16·2	16·3	16·6	571	33·6	34·2	35·1

B. Calculation of [L] *and derivation of the stability constants.*

$C_M' \longrightarrow$ 20	10	5	0				
E_M	C_L	C_L	C_L	$C_L = [L]$	X	X_1	X_2
0·5	26	26	26	26	1·020	0·77	
1·0	51	51	51	51	1·040	0·78	
1·5	77	76	76	76	1·060	0·79	
2·0	102	101	100	100	1·081	0·81	0·50
3·0	153	151	150	149	1·124	0·83	0·47
4·0	203	200	197	197	1·168	0·85	0·46
5·0	253	246	240	238	1·215	0·90	0·59
6·0	299	291	284	282	1·263	0·93	0·60
7·0	346	337	326	322	1·313	0·97	0·65
8·0	395	381	367	360	1·365	1·01	0·69
10·0	490	469	448	440	1·476	1·08	0·73
12·0	582	554	527	516	1·595	1·15	0·76

$\beta_1 = K_1 = 0{\cdot}76 \pm 0{\cdot}05$ l. mole^{-1}; $\beta_2 = 0{\cdot}6 \pm 0{\cdot}2$ l.^{2} mole^{-2}; $K_2 = 0{\cdot}8$ l. mole^{-1}.

titration, but owing to the very small amounts of the second and third complex in the equilibrium mixture (see Fig. 1) the second and third constants (K_2 and K_3) are known only approximately (Tables 6 and 7).

TABLE 4. *The system silver ion–ethylthiobenzenesulphonate ion* ($C_L' = 0{\cdot}03$M; $I = 0{\cdot}1$M).

A. E_M as a function of C_L.

$C_M' \longrightarrow$	10	5	2	$C_M' \longrightarrow$	10	5	2	$C_M' \longrightarrow$	10	5	2
C_L	E_M	E_M	E_M	C_L	E_M	E_M	E_M	C_L	E_M	E_M	E_M
0·395	0·9	1·4	2·5	3·53	8·7	13·8	19·9	10·44	32·5	41·8	48·8
0·779	1·7	2·8	4·8	5·00	13·1	20·0	27·0	13·33	43·5	52·3	58·2
1·154	2·5	4·2	6·9	6·32	17·4	25·5	33·0	17·15	57·5	64·7	69·4
1·875	4·2	6·9	10·9	7·50	21·6	30·3	37·9	18·75	63·3	69·8	—
2·73	6·5	10·5	15·7	8·57	25·6	34·7	42·2				

B. Calculation of [L] *and derivation of the stability constants.*

$C_M' \longrightarrow$	10	5	2	0			
E_M	C_L	C_L	C_L	$C_L = [L]$	X	X_1	X_2
2	0·91	0·55	0·31	0·17	1·081	(480)	
4	1·79	1·10	0·64	0·36	1·169	(470)	
7	2·94	1·90	1·18	0·72	1·313	430	
10	3·96	2·62	1·72	1·11	1·476	430	
15	5·60	3·82	2·60	1·73	1·793	458	
20	7·05	5·00	3·55	2·52	2·178	468	21,000
25	8·42	6·17	4·57	3·40	2·646	484	20,300
30	9·77	7·41	5·63	4·33	3·214	511	22,200
40	12·43	9·97	8·03	6·63	4·745	565	22,600
50	15·10	12·65	10·82	9·32	7·002	644	24,600
60	17·84	15·66	13·95	12·62	10·33	740	25,700

$\beta_1 = 415 \pm 20$ l. mole^{-1}. $K_1 = \beta_1$.
$\beta_2 = (2{\cdot}0 \pm 0{\cdot}2) \times 10^4$ l.^{2} mole^{-2}. $K_2 = 48$ l. mole^{-1}.
$\beta_3 \approx 5 \times 10^5$ l.^{3} mole^{-3}.

TABLE 5. *The system silver ion–*p*-ethylthiobenzenesulphonate ion* ($C_L' = 0{\cdot}2$M; $I = 0{\cdot}2$M).

A. E_M as a function of C_L.

$C_M' \longrightarrow$	10	5	2	$C_M' \longrightarrow$	10	5	2	$C_M' \longrightarrow$	10	5	2
C_L	E_M	E_M	E_M	C_L	E_M	E_M	E_M	C_L	E_M	E_M	E_M
1·32	2·9	4·8	7·3	18·18	44·5	57·1	66·2	57·2	113·0	122·9	129·2
2·64	5·9	9·7	14·3	23·56	56·5	69·1	77·9	63·6	121·5	130·8	137·2
3·92	8·9	14·4	20·3	28·6	66·8	79·1	87·5	69·6	128·7	137·5	
5·20	12·1	19·0	26·1	33·4	75·9	88·1	95·9	80·0	140·5	148·5	
7·70	18·3	27·6	35·7	37·8	83·8	95·6	103·0	88·8	149·7	157·2	
10·14	24·5	35·3	44·0	42·2	90·9	102·4	109·6	100·0	160·5	167·5	
12·52	30·5	42·1	51·4	50·0	102·9	113·5	120·3				

B. Calculation of [L] *and derivation of the stability constants.*

$C_M' \longrightarrow$	10	5	2	0					
E_M	C_L	C_L	C_L	$C_L = [L]$	X	X_1	$10^{-3}X_2$	$10^{-5}X_3$	$10^{-6}X_4$
5	2·25	1·37	0·90	0·55	1·215	391			
10	4·37	2·73	1·82	1·16	1·476	411			
15	6·37	4·11	2·80	1·87	1·793	424			
20	8·35	5·50	3·84	2·68	2·178	439			
30	12·33	8·45	6·18	4·56	3·214	486	21·1		
40	16·35	11·78	8·96	7·00	4·745	535	20·7		
50	20·5	15·50	12·05	10·0	7·002	600	21·0		
60	25·1	19·2	15·5	13·2	10·33	707	24·0	3·8	
70	30·2	24·0	19·8	17·1	15·28	835	26·0	4·1	
80	35·5	29·0	24·7	22·0	22·52	978	26·8	3·5	
90	41·6	34·6	29·9	26·8	33·24	1208	30·6	3·8	
100	48·2	40·6	35·8	32·3	49·04	1487	34·0	4·6	4·3
110	55·0	47·5	42·5	39·2	72·4	1821	36·7	4·5	3·3
120	62·5	54·9	49·9	46·4	106·8	2280	40·8	4·7	3·2
130	70·5	63·0	57·7	53·9	158·4	2920	47·0	5·2	3·7
140	79·5	71·8	66·1	62·5	232·7	3707	53·2	5·5	3·7
150	89·0	81·5	—	72·9	343·5	4720	59·7	5·6	3·3
160	99·4	91·4	—	82·0	507·0	6171	70·6	6·3	3·8

$\beta_1 = 390 \pm 20$ l. mole^{-1}. $K_1 = \beta_1$.
$\beta_2 = (1{\cdot}9 \pm 0{\cdot}2) \times 10^4$ l.^{2} mole^{-2}. $K_2 = 49$ l. mole^{-1}.
$\beta_3 = (3{\cdot}2 \pm 0{\cdot}5) \times 10^5$ l.^{3} mole^{-3}. $K_3 = 17$ l. mole^{-1}.
$\beta_4 = (3{\cdot}6 \pm 0{\cdot}5) \times 10^6$ l.^{4} mole^{-4}. $K_4 = 11$ l. mole^{-1}.

XUM

TABLE 6. *The system silver ion–*p*-phenylthiobenzenesulphonate ion* ($C_L' = 0{\cdot}095$M; $I = 0{\cdot}1$M).

A. E_M as a function of C_L.

$C_M' \rightarrow$	5	2	1	0·5	$C_M' \rightarrow$	5	2	1	0·5	$C_M' \rightarrow$	5	2	1	0·5
C_L	E_M	E_M	E_M	E_M	C_L	E_M	E_M	E_M	E_M	C_L	E_M	E_M	E_M	E_M
0·794	0·8	0·9	0·9	1·0	13·79	13·7	14·8	15·8	16·2	28·6	29·2	31·4	33·4	34·3
2·34	2·4	2·6	2·6	2·8	16·67	16·5	18·0	19·2	19·6	32·4	33·5	35·9	37·7	38·8
3·85	3·8	4·2	4·3	4·5	19·35	19·3	21·0	22·4	22·9	35·9	37·5	40·1	42·0	43·0
5·66	5·7	6·1	6·4	6·6	21·88	22·0	23·7	25·3	26·1	39·0	41·1	43·8	45·9	46·8
7·41	7·3	8·0	8·4	8·7	24·24	24·5	26·5	28·2	29·0	43·2	46·2	48·8	51·1	51·8
10·71	10·6	11·5	12·3	12·6	26·47	26·8	29·0	30·8	31·7	46·8	50·5	53·1	55·7	56·3
										50·0	54·4	57·1	59·6	60·2

B. Calculation of [L] *and derivation of the stability constants.*

$C_M' \longrightarrow$	5	2	1	0·5	0				
E_M	C_L	C_L	C_L	C_L	$C_L = [L]$	X	X_1	$10^{-1}X_2$	$10^{-2}X_3$
2	2·0	1·8	1·7	1·7	1·7	1·081	48		
4	4·0	3·7	3·5	3·4	3·3	1·169	51		
6	6·1	5·6	5·3	5·1	5·1	1·263	52		
8	8·1	7·4	7·0	6·8	6·7	1·366	55		
10	10·1	9·3	8·8	8·5	8·4	1·476	56·7	121	
15	15·2	13·9	13·1	12·7	12·5	1·793	63·5	136	
20	20·1	18·5	17·4	17·1	16·7	2·178	70·7	145	
25	24·7	23·0	21·6	21·0	20·8	2·646	79·1	157	260
30	29·4	27·3	25·7	25·0	24·7	3·214	89·6	174	288
35	33·8	31·7	30·0	29·2	29·0	3·905	100·2	185	283
40	38·1	35·8	34·2	33·3	33·2	4·745	112·8	200	292
45	42·2	40·0	38·3	37·5	37·3	5·762	127·7	218	309
50	46·4	44·2	42·3	41·6	41·3	7·002	145·3	239	329
55	50·5	48·3	46·3	45·7	45·3	8·505	165·6	263	353

$\beta_1 = 47 \pm 2$ l. mole^{-1}. $K_1 = \beta_1$.
$\beta_2 = 1000 \pm 100$ l.^{2} mole^{-2}. $K_2 = 22$ l. mole^{-1}.
$\beta_3 = (13 \pm 4) \times 10^3$ l.^{3} mole^{-3}. $K_3 = 13$ l. mole^{-1}.
$\beta_4 = (5 \pm 2) \times 10^5$ l.^{4} mole^{-4}. $K_4 = 40$ l. mole^{-1}.

TABLE 7. *The system silver ion–*p*-phenylthiobenzenesulphonate ion* ($C_L' = 0{\cdot}2$M; $I = 0{\cdot}2$M).

A. E_M as a function of C_L.

$C_M' \longrightarrow$	5	2	1	$C_M' \longrightarrow$	5	2	1	$C_M' \longrightarrow$	5	2	1
C_L	E_M	E_M	E_M	C_L	E_M	E_M	E_M	C_L	E_M	E_M	E_M
2·6	2·1	2·7	2·9	33·4	32·3	35·7	36·8	69·6	75·4	81·8	84·0
7·7	6·7	7·8	8·2	42·2	42·5	46·6	47·9	80·0	86·6	93·0	95·2
12·5	11·1	12·7	13·3	50·0	52·2	57·1	58·5	88·8	95·2	101·2	103·3
18·2	16·6	18·8	19·5	57·2	60·9	66·5	68·3	100·0	104·7	109·9	111·6
23·6	21·9	24·5	25·4	63·6	68·7	74·8	76·8				

B. Calculation of [L] *and derivation of the stability constants.*

$C_M' \longrightarrow$	5	2	1	0					
E_M	C_L	C_L	C_L	$C_L = [L]$	X	X_1	X_2	$10^{-2}X_3$	$10^{-3}X_4$
3	3·7	2·95	2·7	2·5	1·124	49·5			
5	5·8	4·95	4·6	4·3	1·215	50·0			
7	8·0	6·9	6·5	6·2	1·314	50·6	645		
10	11·25	9·9	9·3	8·9	1·476	53·5	775		
15	16·6	14·65	14·0	13·4	1·793	59·2	940		
20	21·7	19·4	18·7	17·9	2·178	65·8	1073		
30	31·3	28·45	27·6	26·6	3·214	83·25	1378	312	(82)
40	40·55	37·2	36·1	34·9	4·745	107·2	1736	341	(74)
50	48·3	44·7	43·8	42·5	7·002	141·2	2226	396	71
60	56·4	52·2	51·1	49·8	10·33	187·4	2827	457	73
70	64·7	59·9	58·5	56·9	15·28	251·0	3592	534	78
80	73·8	68·0	66·2	64·1	22·51	335·5	4507	616	82
90	83·3	77·2	75·2	73·0	33·24	441·7	5412	665	79
100	94·4	87·7	85·0	82·4	49·20	584·9	6533	726	77
105	100·5	93·4	90·9	88·2	59·6	664·0	7000	731	73

$\beta_1 = 47 \pm 2$ l. mole^{-1}. $K_1 = \beta_1$.
$\beta_2 = 550 \pm 100$ l.^{2} mole^{-2}. $K_2 = 12$ l. mole^{-1}.
$\beta_3 = (9 \pm 4) \times 10^3$ l.^{3} mole^{-3}. $K_3 = 16$ l. mole^{-1}.
$\beta_4 = (7{\cdot}5 \pm 2) \times 10^5$ l.^{4} mole^{-4}. $K_4 = 85$ l. mole^{-1}.

TABLE 8. *The system silver ion–dianion of di-(p-sulphophenyl) sulphide* ($C_L' = 0{\cdot}0667$M; $I = 0{\cdot}2$M).

A. E_M as a function of C_L.

$C_M' \longrightarrow$	5	2	$C_M' \longrightarrow$	5	2	$C_M' \longrightarrow$	5	2
C_L	E_M	E_M	C_L	E_M	E_M	C_L	E_M	E_M
0·53	0·3	0·4	11·12	6·7	6·8	23·93	14·8	15·3
1·56	1·0	1·0	12·91	8·0	8·0	26·03	16·1	16·6
2·57	1·5	1·6	14·59	9·0	9·1	28·80	17·9	18·5
3·78	2·2	2·4	16·17	10·0	10·2	31·22	19·4	20·2
4·94	3·0	3·1	17·66	10·9	11·1	33·35	20·8	21·6
7·14	4·4	4·5	19·05	11·8	12·0			
9·20	5·6	5·8	21·63	13·3	13·7			

B. Calculation of [L] *and derivation of the stability constants.*

$C_M' \longrightarrow$	5	2	0				
E_M	C_L	C_L	$C_L = [L]$	X	X_1	X_2	X_3
2	3·2	3·2	3·2	1·081	25·3		
4	6·5	6·3	6·4	1·168	26·3		
6	9·8	9·6	9·5	1·263	27·7	284	
8	13·0	12·8	12·7	1·365	28·7	291	
10	16·2	15·9	15·7	1·476	30·6	338	8800
12	19·5	19·1	18·8	1·595	31·6	351	8000
14	22·6	22·0	21·6	1·725	33·6	398	9200
16	25·8	25·1	24·6	1·864	35·1	411	8600
18	29·0	28·1	27·5	2·015	36·9	433	8500
20	32·2	31·0	30·1	2·178	39·1	468	8900
22	35·4	34·0	33·1	2·354	40·9	480	8500

$\beta_1 = 25 \pm 2$ l. mole^{-1}. $K_1 = \beta_1$.
$\beta_2 = 200 \pm 30$ l.^{2} mole^{-2}. $K_2 = 8$ l. mole^{-1}.
$\beta_3 = 8500 \pm 1000$ l.^{3} mole^{-3}. $K_3 = 44$ l. mole^{-1}.

TABLE 9. *The system silver ion–p-phenylselenobenzenesulphonate ion* ($C_L' = 0{\cdot}1$M; $I = 0{\cdot}1$M).

A. E_M as a function of C_L.

$C_M' \longrightarrow$	2	1	0·5	$C_M' \longrightarrow$	1	0·5	$C_M' \longrightarrow$	1	0·5
C_L	E_M	E_M	E_M	C_L	E_M	E_M	C_L	E_M	E_M
0·66	4·2	5·2	6·1	6·26	43·5	48·2	25·0	132·2	137·8
1·32	8·2	10·1	11·9	7·41	50·6	55·8	28·6	114·5	149·7
1·96	11·9	14·8	17·2	9·09	60·7	66·3	31·8	154·9	159·9
2·60	15·7	19·5	22·2	11·78	75·3	81·3	34·8	163·8	168·6
3·23	19·4	23·8	27·1	14·3	87·9	93·9	40·0	178·5	182·9
3·85	23·0	27·9	31·6	16·7	99·0	105·2	44·4	190·1	194·4
4·46	26·4	—	—	18·9	108·7	114·7	50·0	203·8	207·7
5·07	—	36·1	40·3	21·1	117·3	123·3			

B. Calculation of [L] *and derivation of the stability constants.*

$C_M' \longrightarrow$	2	1	0·5	0					
E_M	C_L	C_L	C_L	$C_L = [L]$	X	X_1	$10^{-3}X_2$	$10^{-4}X_3$	$10^{-6}X_4$
5	0·78	0·63	0·54	0·46	1·215	467			
10	1·62	1·29	1·11	0·95	1·476	501			
15	2·49	1·98	1·20	1·44	1·793	551	84·1		
20	3·34	2·67	2·31	1·92	2·178	598	85·3		
25	4·21	3·41	2·96	2·54	2·646	648	84·9		
30		4·16	3·63	3·10	3·214	714	91·7	4·42	
40		5·69	5·04	4·38	4·245	855	97·2	4·38	
50		7·31	6·53	5·75	7·002	1044	106·7	4·99	4·16
60		9·0	8·1	7·2	10·33	1296	120·3	5·88	4·56
75		11·7	10·65	9·6	18·53	1826	145·4	7·02	4·61
90		14·75	13·55	12·35	33·24	2610	176·6	7·98	4·37
100		16·95	15·6	14·25	49·04	3370	206·5	9·02	4·51
110		19·3	17·8	16·3	72·4	4380	242·5	10·09	4·59
120		21·85	20·25	18·65	106·8	5670	281	10·89	4·44
135		25·8	24·2	22·6	191·6	8430	354	12·22	4·27
150		30·25	28·75	27·2	343·5	12,600	447·5	13·6	4·04
160		33·5	31·9	30·3	507·0	16,720	538	15·2	4·17
170		36·95	35·3	33·65	748	22,220	648	16·95	4·27
180		40·55	39·0	37·45	1105	29,470	776	18·65	4·29
190		44·3	42·7	41·1	1630	39,650	954	21·35	4·57
200		48·3	46·8	45·3	2405	53,150	1164	24·0	4·72

$\beta_1 = 430 \pm 20$ l. mole^{-1}. $K_1 = \beta_1$.
$\beta_2 = (7{\cdot}8 \pm 0{\cdot}7) \times 10^4$ l.^{2} mole^{-2}. $K_2 = 180$ l. mole^{-1}.
$\beta_3 = (2{\cdot}6 \pm 0{\cdot}5) \times 10^6$ l.^{3} mole^{-3}. $K_3 = 33$ l. mole^{-1}.
$\beta_4 = (4{\cdot}4 \pm 0{\cdot}7) \times 10^8$ l.^{4} mole^{-4}. $K_4 = 170$ l. mole^{-1}.

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The disodium salt of di-(*p*-sulphophenyl) sulphide was prepared in order to provide a derivative of diphenyl sulphide more soluble in water than the monosulphonate. In this way it was hoped to obtain the higher constants more accurately than was possible with the monosulphonate, but unfortunately the disulphonate was so weak a complexing agent that only three constants could be obtained (Table 8). It appears as if the formation of complexes ceases at $\bar{n} = 3$ (*i.e.*, that X_3 is constant). This may well be so since the ionic charge on the complex $[Ag\{S(C_6H_4 \cdot SO_3^-)_2\}_3]^{5-}$ would strongly repel the addition of a fourth molecule of the disulphonate, but at a higher concentration of free ligand, had solubility allowed it, the formation of complexes might have continued.

Sodium *p*-phenylselenobenzenesulphonate had sufficient affinity for silver ion to allow the whole range of complex formation to be covered at $I = 0{\cdot}1$M, but even at such a low ionic strength only very dilute solutions of silver perchlorate could be investigated. Three concentrations were used $C_M' = 0{\cdot}5$ mM, 1 mM, and 2 mM. The *silver salt* was precipitated from the 2mM-solution when the concentration of ligand reached 4·5 mM (Found: Ag, 25·6. $C_{12}H_9O_3SAgSe$ requires Ag, 25·7%). At the lower concentrations no precipitation occurred up to ligand concentrations of 50 mM. The results are listed in Table 9.

Appendix

Leden's Method[3] *as Modified by Fronaeus*[10] *for Determination of Stability Constants.*— In an aqueous solution containing a metal ion, M, and a ligand, L, a series of mononuclear complexes ML, ML_2 . . . ML_N may exist in equilibrium with the hydrated metal ion and the ligand. The total concentration of the metal ion (C_M) both free and in complexes is given by

$$C_M = [M] + [ML] + [ML_2] \ldots . + [ML_N] \quad . \quad . \quad . \quad . \quad . \quad (1)$$

Using the definition of the gross concentration stability constants β_1, β_2, etc., on p. 265 we obtain a function X such that

$$C_M/[M] = 1 + \beta_1[L] + \beta_2[L]^2 \cdots \cdots \cdots \beta_N[L]^N = X \quad . \quad . \quad . \quad (2)$$

Provided X and [L] are known over the whole range of complex formation by L then all the β's can be determined as follows. A new function X_1 is formed from eqn. (2) such that

$$X_1 = (X - 1)/[L] = \beta_1 + \beta_2[L] + \beta_3[L]^2 \cdots \cdots \beta_N[L]^{N-1}. \quad . \quad . \quad (3)$$

If X_1 is now plotted against [L] and extrapolated to cut the X_1 axis we obtain β_1 as the intercept and β_2 as the slope at the point of intersection. However, β_2 is better obtained by writing a new function X_2 similar to X_1 such that

$$X_2 = (X_1 - \beta_1)/[L] = \beta_2 + \beta_3[L] + \cdots \cdots \beta_N[L]^{N-2}. \quad . \quad . \quad . \quad (4)$$

and so obtaining β_2 which is the limiting value of X_2 as $[L] \longrightarrow 0$. The higher constants (β_3, β_4, etc.) are calculated analogously until finally a constant function $X_N = \beta_N$ is found. This indicates that ML_N is the highest complex formed in the range of concentrations used.

The values of X and [L] needed for the above calculation are found by determining the e.m.f. of the following cell with various total concentrations of metal ion, C_M, and ligand C_L, in the right-hand compartment.

	+			−
Reference electrode	Bridge	Metal ion (C_M) Ligand (C_L) Ionic medium (I, $NaClO_4$)		M,MCl (or M,MBr)

The e.m.f., E, is given by

$$E = E_k + (RT/nF) \ln [M] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

where E_k includes the potential of the reference electrode, the liquid junction potentials, and activity coefficients, *i.e.*, all factors considered to remain constant throughout the

measurements. When $C_L = 0$, *i.e.*, no ligand has been added to the cell, the e.m.f., E_0, is given by

$$E_0 = E_k + (RT/nF) \ln C_M \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

The addition of ligand to the cell gives a new potential E, and the difference $E_0 - E$ gives X directly according to (7).

$$E_0 - E = E_M = (RT/nF) \ln (C_M/[M]) = (RT/nF) \ln X \quad . \quad . \quad . \quad (7)$$

Since X is a function only of [L] [eqn. (2)] and E_M is a function only of X, there is for every E_M a unique value of [L], independent of the total metal concentration, C_M. To find corresponding values of E_M and [L], E_M is determined experimentally as a function of C_L at several values of C_M. A family of curves is then obtained (Fig. 3) where $C_M'''' > C_M''' > C_M'' > C_M'$. These curves are cut at a number of values of E_M, and C_M plotted against C_L for every E_M (Fig. 4). By extrapolation to $C_M = 0$, [L] (which is equal to C_L at $C_M = 0$) is found for each particular value of E_M, as the intercept on the C_L axis.

FIG. 3.

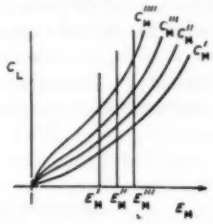
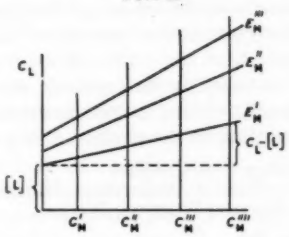


FIG. 4.



From this X is determined as a function of [L], and so the constants β_1, β_2, etc., from the eqns. (3), (4), etc.

X as a function of [L] can be determined in this manner only when the ligand has a weak or moderate affinity for the metal ion (*i.e.*, $\beta_1 \lessapprox 1500$ l. mole^{-1}), as is the case here. If the affinity is strong (*i.e.*, $\beta_1 \gtrapprox 1500$ l. mole^{-1}), [L] is so low when the formation of complexes takes place (or at least during the formation of the lower complexes), that the extrapolations pass too close to the origin to allow reliable values of [L] to be read. In such cases an alternative procedure described in the Appendix of Part II (following paper) has to be used.[10]

From the fact that [L] is constant along a line of constant E_M it follows that the ligand number $\bar{n}$, defined according to eqn. (8)

$$\bar{n} = (C_L - [L])/C_M \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

is constant too. For when eqns. (9)

$$C_L = [L] + \sum_{n=1}^{N} n[ML_n] = [L] + [M] \sum_{n=1}^{N} n\beta_n[L]^n \quad . \quad . \quad . \quad . \quad (9)$$

and (2) are inserted in (8) we obtain

$$\bar{n} = \frac{\sum_{n=1}^{N} n\beta_n[L]^n}{1 + \sum_{n=1}^{N} \beta_n[L]^n} = \frac{\sum_{n=1}^{N} n\beta_n[L]^n}{X} \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

i.e., $\bar{n}$ is a function of [L] only, and therefore constant along a line of constant [L]. Thus, at constant E_M, the relation (8) between C_L and C_M must be a straight line with the slope $= \bar{n}$, corresponding to the value of [L] found as the intercept in Fig. 3.

From the constants β_1, β_2, etc., so obtained it is possible to calculate the fraction α_n of the total metal concentration which is present in the form of each particular complex ML_n in equilibrium at each value of [L] by using equation (11):

$$\alpha_n = \frac{[ML_n]}{C_M} = \frac{\beta_n[L]^n}{X} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

By plotting the mole percentage of silver in the various complexes against log [L] it is possible to see graphically the regions of stability of each complex (Fig. 1).[26]

In the derivation of the above equations we have assumed that only mononuclear complexes are formed. If polynuclear complexes are formed as well, E_M depends on both [L] and [M], but it has been shown [10] that the intercept on the C_L axis still gives [L] corresponding to the value of X found according to eqn. (7). However, the slope of the C_L–C_M curve will then be a quantity $<\bar{n}$. Nevertheless, as X can be found as a function of [L] it is still possible to determine the stability constants of the mononuclear complexes present, and hence the true values of $\bar{n}$ according to eqn. (10). Comparison of the $\bar{n}$'s thus found with those obtained from the slopes reveals whether polynuclear complexes are formed. In our experiments we found no evidence of polynuclear complex formation.

This test for polynuclear complexes fails when a great enough range of C_M is not available, because then the curves giving E_M as a function of C_L are close together and the C_L–C_M slopes cannot be determined with any certainty. Nevertheless, the correct stability constants relating to the formation of the mononuclear complexes can still be determined according to the method above.

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[26] Cf. ref. 2, p. 287.

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55. *The Relative Affinities of Co-ordinating Atoms for Silver Ion. Part II.*[1] *Nitrogen, Phosphorus, and Arsenic.*[2]

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The stability constants of some sulphonated anilines, a sulphonated triphenylphosphine and a sulphonated triphenylarsine with silver(I) ion have been determined in aqueous solution. The affinity of silver ion (as ΔG°) for the phosphine is some 10 kcal. mole^{-1}, and for the arsine 6 kcal. mole^{-1}, greater than for the anilines. The shapes of the complex-formation curves of a wide variety of ligands with silver ion are remarkable for their variety, and because few of them have the "stop" or inflection, hitherto considered characteristic of silver ion, at $\bar{n} = 2$. The shapes are interpreted in terms of d_π-bonding by the co-ordinating atoms. They indicate that the d_π-bonds formed by the phosphine, arsine, and iodide ion are strong compared with those formed by sulphides and selenides, and by chloride ion and bromide ion.

STABILITY constants of a sulphonated aromatic ether, three sulphonated aromatic sulphides, and a selenide with silver ion are known.[1] We now describe corresponding measurements for the sulphonated amines, phosphine, and arsine listed in Table 1 together with their stability constants. The experimental method and notation are those of Part I except that the highly complex-forming phosphine and arsine necessitated Ag–AgI electrodes for measuring the concentration of silver ion at high ligand concentrations, and indeed even

[1] Part I, preceding paper.
[2] This work was briefly reported at the 10th Solvay Conference (1956), and in *Nature*, 1957, **179**, 1187.

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these electrodes were stripped of their silver iodide at the highest concentration of phosphine tried. The constants for the amines were calculated by Leden's method as developed by Fronaeus;[3] as this could not be used for the phosphine and arsine Fronaeus's alternative method (Appendix) was used.

The sulphonated ligands used are not exactly analogous but the differences between their constants are so great that there can be no doubt about the relative affinities of similar amines, phosphines, and arsines for silver ion.

TABLE 1. *Concentration stability constants, K (l. mole^{-1}) of the ligands, L, with silver ion at an ionic strength I* (M) *and* 25°.

L	I	K_1	K_2	K_3	K_4	log K_1
p-$H_2N{\cdot}C_6H_4{\cdot}SO_3^-$	0·1	13·7	9	—	—	1·14
	1	10·7	4·4	2·5	0·8	1·03
p-$Me_2N{\cdot}C_6H_4{\cdot}SO_3^-$	0·1	5·7	4	—	—	0·76
m-$H_2N{\cdot}C_6H_4{\cdot}SO_3^-$	1	17	8	1·5	1·3	1·23
m-$Ph_2P{\cdot}C_6H_4{\cdot}SO_3^-$	0·1	$1{\cdot}4 \times 10^8$	$0{\cdot}9 \times 10^6$	$2{\cdot}5 \times 10^5$	—	8·15
$As(C_6H_4{\cdot}SO_3^-{-}m)_3$	0·2	$2{\cdot}3 \times 10^5$	—	—	—	5·36

The tendency of silver ion to form its strongest complexes with the second or a subsequent, rather than with the first, co-ordinating atom in each Group is evidently very marked in Group V.

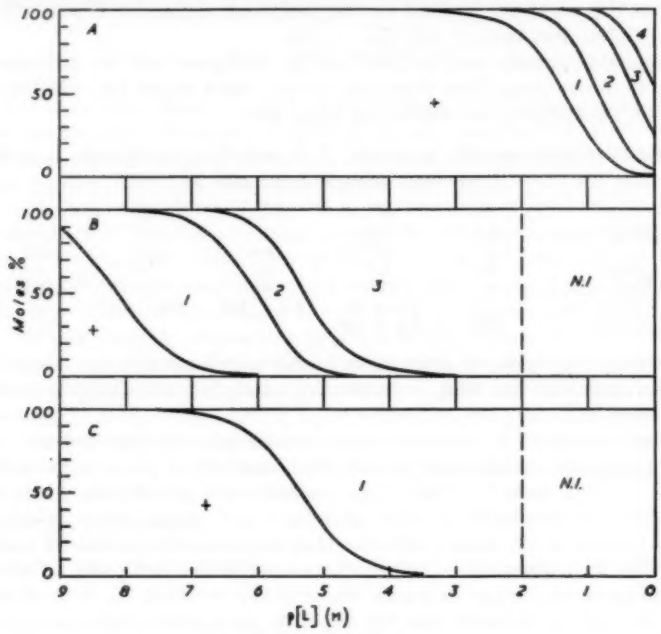
The highest constants K_1 for unidentate amines (*e.g.*, ethylamine) are $<2{\cdot}5 \times 10^3$, whereas the phosphine has the exceptionally high constant of $1{\cdot}4 \times 10^8$ l. mole^{-1} and the arsine of $2{\cdot}3 \times 10^5$ l. mole^{-1}. These high constants are remarkable when we consider that they refer to a completely aromatic phosphine and similar arsine, which are known qualitatively to have much weaker affinities than aliphatic derivatives for most acceptor atoms. In Part I we observed that the replacement of the phenyl by an ethyl group in *p*-phenylthiobenzenesulphonate increases the stability constant K_1 with silver ion by a factor of 9, so it seems probable that the aliphatic phosphines might have first stability constants a few orders greater than 10^8. Sulphonation weakens the co-ordinating affinity of *p*-phenylthiobenzenesulphonate [1] ion and of aniline (see below) by a factor of about 2 in the stability constant, so it seems likely that an arsine strictly comparable with the diphenylphosphinobenzenesulphonate ion would have a constant K_1 of about 10^6 l. mole.$^{-1}$

The complex between silver ion and the monosulphonated triphenylarsine would thus be weaker than its phosphorus analogue by a factor of about 100 in K_1. This contrasts with the situation when the co-ordinating atoms belong to Groups VI and VII; the selenide and bromo-complexes of silver(I) are stronger than their sulphide and chloro-analogues respectively (Fig. 2). Nevertheless, it is in keeping with all qualitative evidence regarding the relative stabilities of tertiary arsine and phosphine complexes. There appears to be no example of a complex compound which, with arsenic as its co-ordinating atom, is more stable than its phosphorus analogue.

The sulphonated amines are exceptionally weak, as amines, in their co-ordinating affinities for silver ion, largely because the lone pair of electrons on the nitrogen atom is strongly conjugated with the aromatic system. This may be seen on comparing ethylamine [4] ($K_1 = 2340$ l. mole^{-1} in 0·5M-KNO_3 at 25°) with aniline [5] ($K_1 = 27{\cdot}5$ in 0·5M-KNO_3 at 25°). The sulphonate ion group must account for the further slight weakening compared with aniline. The values of the stability constants (K_1, Table 1) of the sulphanilate and metanilate are in the sequence expected from their affinities for hydrogen ion (reciprocal of their acid dissociation constants) but the constant K_1 of the *NN*-dimethylsulphanilate is relatively much smaller ($1/K_a$ at $I = 0$ and 25°; sulphanilic acid [6] $1{\cdot}6 \times 10^3$, dimethylsulphanilic acid $4{\cdot}0 \times 10^3$; metanilic acid [6] $5{\cdot}0 \times 10^3$). Such weakening of an amine

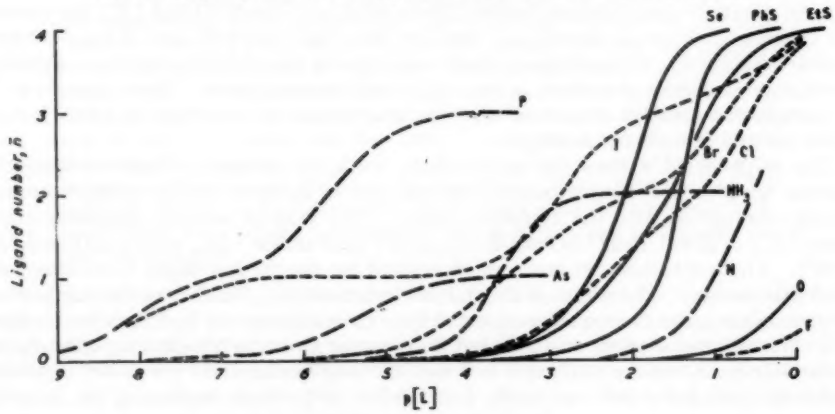
[3] Fronaeus, "Komplexsystem hos Koppar," Gleerupska Univ.-Bokhandeln, Lund, 1948. See Appendix to Part I.
[4] Bruehlman and Verhoek, *J. Amer. Chem. Soc.*, 1948, **70**, 1401.
[5] Golombic, *ibid.*, 1952, **74**, 5777.
[6] Beilstein's Handbuch, H 689, 696; E I 718, 720.

FIG. 1. *Regions of stability of the complex ions* AgL_n *showing the percentages of the total silver content in the form of the various complexes and their variation with* [L] *at 25°.*



A. L = *m*-H_2N-C_6H_4-SO_3^-; I = 1M.
B. L = *m*-Ph_2P-C_6H_4-SO_3^-; I = 0·1M.
C. L = $As(C_6H_4\text{-}SO_2^-\text{-}m)_3$; I = 0·2M.
N.I., not investigated.

FIG. 2. *Complex-formation curves of silver ion with various unidentate ligands.*



——— Group V co-ordinating atoms (N, P, As).
——— Group VI co-ordinating atoms and groups (O, SEt, SPh, Se).
– – – – – Group VII co-ordinating ions (F^-, Cl^-, Br^-, I^-).

towards complex formation with a metal, compared with hydrogen ion, is usually observed on its complete alkylation.[7]

The sulphanilate and metanilate ion systems are remarkable in that there is no sign of a stop in complex formation at $\bar{n}$ (ligand number) $= 2$; previous workers have never reported any evidence that aqueous systems of a monoamine and silver ion contain any other than the species AgL and AgL_2; this is the first record of the types AgL_3 and AgL_4.

None of the systems which we have investigated shows any stop in the formation of silver complexes at $\bar{n} = 2$. This is emphasised in the diagrams (Fig. 1) which show the regions of stability of the various complexes. They indicate that the AgL_2 type of complex has no more than an average region of stability and in the case of the phosphine it has by far the smallest region of stability. In the case of the arsine complex the region of the second complex, if it exists, was not reached.

Our measurements, together with Leden's,[8] supply quantitative data concerning the formation of silver ion complexes with a greater variety of co-ordinating atoms than are available for any other metal ion or acceptor molecule. In Fig. 2 the formation curves are shown together with Bjerrum's [9] curve for ammonia. The variety of shapes of formation curves could hardly be greater. They are of three main types: (1) those (NH_3, Cl, Br) which have a stop or inflection at $\bar{n} = 2$; (2) an intermediate type (S, Se) where the formation of complexes proceeds uniformly to $\bar{n} = 4$; and (3) those (P, As, I) with a stop or inflection at $\bar{n} = 1$ and $\bar{n} = 3$. Cyanide,[10] azide,[11] and thiocyanate [12] ions also give curves of type (1).

Until now type (1) has been considered characteristic of silver ion, and generally amines appear to have formation curves of this type.[4] Nevertheless, the sulphonated anilines have curves of type (2), and further investigation may show this to be true of other amines, particularly aromatic amines. Evidently the linear AgL_2 type of complex whose special stability would cause an inflection at $\bar{n} = 2$ is not favoured by phosphorus, sulphur, selenium, or iodide ion as co-ordinating atoms, or even by nitrogen in the sulphonated amines. Probably arsenic, antimony, and tellurium will behave similarly to phosphorus, sulphur, and selenium. Evidently silver(I) can no longer be regarded as having a characteristic co-ordination number of 2, which is sometimes supplemented by further addition of one or two weakly held ligands. In fact, silver(I) changes its co-ordination number according to the nature of the co-ordinating atoms: 4 is found for more types of co-ordinating atoms than either 2 or 3, so if any is to be considered as characteristic of silver it must be 4. Perhaps it is better to recognise that silver has no characteristic co-ordination number but that the number of unidentate ligand molecules which can be accommodated by silver ion is very sensitive to the nature of the co-ordinating atoms.

The shapes of the formation curves appear to be connected with the d_π-bonding characteristics of the co-ordinating atoms.

The accumulation of qualitative evidence now suggests that with transition-metal ions such as platinum(II) and silver(I), the tendencies of the co-ordinating atoms in their alkyls to form d_π-bonds increase in the order amines $<$ selenides $\sim$ sulphides $<$ arsines $<$ phosphines [13,14] and of the halide ions in the order Cl $<$ Br $<$ I.[15,16]

The chloride and bromide ions probably fit into the first series near the selenides, or in

[7] Chatt and Gamlen, *J.*, 1956, 2371.
[8] Leden, *Svensk kem. Tidskr.*, 1953, **65**, 88; *Z. Naturforsch.*, 1953, **8a**, 719; *Acta Chem. Scand.*, 1956, **10**, 812.
[9] Bjerrum, "Metal Ammine Formation in Aqueous Solution," P. Haase and Son, Copenhagen, 1941, p. 131.
[10] Jones and Penneman, *J. Chem. Phys.*, 1954, **22**, 965.
[11] Leden and Schöön, *Trans. Chalmers Univ. Technology*, Nr. 144, 1954.
[12] Leden and Nilsson, *Z. Naturforsch.*, 1955, **10a**, 67.
[13] Ahrland and Chatt, *J.*, 1957, 1379 and references quoted therein.
[14] Chatt, Duncanson, and Venanzi, *J.*, 1955, 4461.
[15] Chatt, Duncanson, and Venanzi, *J.*, 1956, 2712 and references quoted therein.
[16] Chatt and Wilkins, *J.*, 1956, 525.

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the case of chloride between the amines and selenides. The iodide ion probably fits between the arsines and phosphines.

The selenides and sulphides and the chloride ion appear to have only a slight tendency to form d_π-bonds, and the arsines a definitely lower tendency than the phosphines. The d_π-bonding tendencies of sulphides are thus lower than was originally supposed.[17] Our evidence for the above order is mainly from equilibria and infrared spectroscopy. The low position of the sulphide is in agreement with Backhouse, Foss, and Nyholm's observation that dialkyl and alkyl aryl sulphides do not cause electron pairing in nickel(II),[18] and of the arsines relative to the phosphines by our recent observation that the acetylene $C_2(p\text{-}C_6H_4\cdot NO_2)_2$ (ac) will displace the chelate $o\text{-}C_6H_4(AsMe_2)_2$ from $[o\text{-}C_6H_4(AsMe_2)_2PtPPh_3]^0$ in preference to the unidentate PPh_3 to give $[(Ph_3P)_2Pt\ ac]$ as a product. In a low valency state such as Pt(0) d_π-bonding doubtless contributes substantially to stabilise the Pt–P bond.[19]

Against this background it can be seen that the ligands with little or no d_π-bonding capacity have formation curves of type 1 tending to type 2; those of rather more d_π-bonding capacity have type 2 and those of still greater d_π-bonding capacity have type 3. p_π-Bonding capacity on the part of the co-ordinating atom does not alter the shape of the formation curve in the same manner; thus CN forms stable $[Ag(CN)_2]^-$ ions as well as higher species. The fact that the thiocyanate ion has a curve of type 1 suggests that the $[Ag(SCN)_2]^-$ species in solution is an equilibrium mixture having Ag–N as well as Ag–S bonds.[20]

The way in which d_π-bonding on the part of co-ordinating atoms can affect the shape of the formation curve can be explained if we suppose that in the absence of d_π-bonding the linear AgL_2 ion such as occurs in solid salts of $[Ag(NH_3)_2]^+$ and $[Ag(CN)_2]^-$ is particularly stable. The first ligand molecule to be attached to the aquated silver ion to give the aquated complex, AgL, will have its attachment strengthened by any dative π-bonding from metal to ligand which might occur. d_π-Bonding by the ligand atom on the x co-ordinate would involve the d_{xy}- and d_{xz}-orbitals of the metal probably hybridised with the p_y- and p_z-orbitals respectively. These orbitals and electrons in them would also have to be used for d_π-bonding to a second ligand molecule if it were attached in the diametrically opposite position to the first. However, since they are already used in bonding to the first they are not so readily available for the second and so its attachment will be delayed. Indeed, if d_π-bonding by the ligand atom contributes significantly to bond strength, the second ligand molecule may not attach itself at all in the diametrically opposed position, but rather in a trigonal or tetrahedral position. It can be seen that strong d_π-bonding on the part of the co-ordinating atom will lower the stability of the linear complex, AgL_2, and increase that of the first complex, AgL; hence the inflection at $n = 1$, when strong d_π-bonding occurs to the ligand atom.

The reason for the inflection at $\bar{n} = 3$ in the case of the stronger d_π-bonding ligands is not so clear. It may be connected with the combination of the p_x- with the d_{xz}- and d_{yz}-orbitals of the silver ion to give three trigonally directed π-type orbitals, but electrons are available from the d_{xz}- and d_{yz}-orbitals to form only two strong π-type bonds with the ligands.[21] It seems unlikely that this would lead to a very stable trigonal complex, although it may be stabilised relative to the linear complex. In the case of the phosphine complex steric effects are probably largely responsible for the stop in complex formation at $\bar{n} = 3$.

Strong p_π-bonding by the co-ordinating atoms should not lead to curves of type 3. In such a case the attachment of the first ligand molecule will involve only the electrons from one d-orbital on the silver ion, say the d_{xy}, and so those from the d_{xz}-orbital will

[17] Cf. Chatt and Williams, *J.*, 1951, 3061.
[18] Backhouse, Foss, and Nyholm, *J.*, 1957, 1714.
[19] Chatt, Rowe, and Williams, *Proc. Chem. Soc.*, 1957, 208.
[20] Cf. Lindqvist and Strandberg, *Acta Cryst.*, 1957, **10**, 173.
[21] Chatt and Ahrland, *Chem. and Ind.*, 1955, 96.

remain available to attach the second ligand molecule in the diametrically opposed position. Thus the special stability of the linear AgL_2 type of complexes is not destroyed by p_π-bonding on the part of the ligand atom as the existence of the stable $[Ag(CN)_2]^-$ ion shows.

The great variety of formation curves formed by the various ligand molecules with silver ion is as much a property of the silver ion as of the ligand atoms. They arise because silver ion can form stable complexes of linear sp, trigonal sp^2, and tetrahedral sp^3 hybridisations, and the solution could contain an equilibrium mixture of hydrated ions of these types. The relative stabilities of these will be altered markedly by the electronegativities, and d_π-type bonding characteristics of the co-ordinating atoms, especially the stability of the AgL_2, will be decreased, and those of all forms of AgL increased, by d_π-bonding. Our experiments indicate also that the stability of AgL_3 is increased relative to AgL_2 by d_π-bonding.

This work was started with the object of determining the relative d_π-bonding capacities of the various donor atoms of Groups V and VI by observing the stabilisation of the AgL type of complex relative to the AgL_2, but then we did not expect to find evidence of species other than $Ag(H_2O)_2$, AgL,H_2O, and AgL_2. The existence of further complexes complicates the situation, but the ratio K_1/K_2 may nevertheless supply some rough measure of the relative d_π-bonding capacities of analogous ligands of the same charge. When ligands carry a higher charge, such as $S(C_6H_4\cdot SO_3^-)_2$ or more especially $As(C_6H_4\cdot SO_3^-)_3$, the electrostatic repulsion of the ligands may have a great additional influence on the value of K_1/K_2. Indeed, for the arsine we have no evidence that more than one ligand was ever taken up over the range of concentrations studied. The ratios K_1/K_2 are given in Table 2.

TABLE 2. *The ratio K_1/K_2 for silver ion with a number of ligands containing co-ordinating atoms from Groups V, VI, and VII at* 25° (NH_3, 22°).

L	I	K_1/K_2	L	I	K_1/K_2
Group V			Group VII		
NH_3	2·0	0·3			
p-$H_2N\cdot C_6H_4\cdot SO_3^-$	0·1	1·5	Cl^-	0·2	9
	1	2·4		5	6
p-$Me_2N\cdot C_6H_4\cdot SO_3^-$	0·1	1·4	Br^-	0·1	15
m-$H_2N\cdot C_6H_4\cdot SO_3^-$	1	2·1		5	≈20
m-$Ph_2P\cdot C_6H_4\cdot SO_3^-$	0·1	160	I^-	4	≈10^5
Group VI			Polysulphonates		
p-$MeO\cdot C_6H_4\cdot SO_3^-$	1	1	$As(C_6H_4\cdot SO_3^-$-$m)_3$	0·2	>10^4
p-$EtS\cdot C_6H_4\cdot SO_3^-$	0·1	9	$S(C_6H_4\cdot SO_3^-$-$p)_2$	0·2	3
	0·2	8			
p-$PhS\cdot C_6H_4\cdot SO_3^-$	0·1	2·1			
	0·2	3·9			
p-$PhSe\cdot C_6H_4\cdot SO_3^-$	0·1	2·4			

The ratios (K_1/K_2) of the phosphine and iodide ion are by far the highest amongst ligands of their respective types. This agrees with all our previous experience of the complex chemistry of platinum(II) and palladium(II) with phosphines and iodide ion as ligands, *viz.*, that the d_π-bonding capacity of a phosphine appears to be greater than that of all other ligand atoms in similar circumstances of combination (AsR_3, SR_2, etc.) and that of iodide ion is much greater than that of the other halide ions.

EXPERIMENTAL

Microanalyses are by Messrs. W. Brown and A. G. Olney, of these laboratories.

Preparation of Ligands.—The three sulphonates derived from aniline were commercial products recrystallised from water until analyses (C and H) and equivalent weights were correct.

Sodium diphenylphosphinobenzene-m-*sulphonate.* Triphenylphosphine (10 g.) was added slowly with cooling to a mixture of 20% SO_3–H_2SO_4 (19 c.c.) and 65% SO_3–H_2SO_4 (1 c.c.).

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The phosphine dissolved and the solution was heated on a water-bath. The solution was tested at intervals by adding one drop to water (2—3 c.c.) until a test drop gave a clear or only slightly cloudy aqueous solution (½—2 hr. depending on the acid strength). The acid solution was cooled, poured cautiously into water (200 c.c.) and neutralised with saturated sodium hydroxide solution. The product separated as fine, white, shining leaves. This may be contaminated by large crystals of sodium sulphate if the solution is allowed to stand too long or is chilled in ice. It was centrifuged off and the soluble part extracted with water. The aqueous extract was evaporated at 100° to crystallisation and cooled; the crystalline product which separated was recrystallised from a small amount of ethyl alcohol (yield 5 g.). Recrystallised from water and dried (50% sulphuric acid), it gave the *dihydrate* (Found: equiv. by ion exchange, 401, 404. $C_{18}H_{14}O_3SPNa,2H_2O$ requires equiv., 400). It was characterised as its *benzylisothiuronium salt*, m. p. 146—148° (Found: C, 61·15; H, 5·0; N, 5·5. $C_{26}H_{26}O_3N_2SP$ requires C, 61·4; H, 4·95; N, 5·5%).

Trisodium salt of tri-(m-*sulphophenyl*)*arsine* (*trisodium triphenylarsine*-mm′m″-*trisulphonate*). Triphenylarsine (20 g.) in 65% SO_3–H_2SO_4 (30 c.c.) was heated on a water-bath for 1½ hr., then poured into water (250 c.c.), and the slight insoluble precipitate which formed was filtered off. The filtrate contains $Na_3[AsO(C_6H_4{\cdot}SO_3)_3]$.[22] This arsine oxide was reduced by addition of concentrated hydrobromic acid (150 c.c.) and a few crystals of potassium iodide followed by passage of sulphur dioxide for 19 hr. The dissolved sulphur dioxide was then removed by blowing nitrogen through the solution for 5½ hr. The solution was neutralised with barium hydroxide and finally barium carbonate, the precipitated sulphate was removed from the hot solution and the filtrate taken to dryness.

The white residue was extracted with methanol in a Soxhlet apparatus for 6 hr. to remove barium bromide, ground, and then extracted further with methanol (100 c.c.). To remove the last traces of bromide, the solid was dissolved in the minimum amount of hot water and reprecipitated with a large excess of methanol. The filtered precipitate was then dissolved in hot water (150 c.c.) and caused to crystallise by the addition of methanol (100 c.c.) and cooled. The pure hygroscopic barium salt (8·7 g.) separated, and was converted into the *sodium salt* as previously described, then dried at 130° [23] (Found: C, 34·1; H, 2·3%; equiv., 203. $C_{18}H_{12}O_9S_3AsNa_3$ requires C, 33·7; H, 2·0%; equiv., 204).

Orientation of the sulphonated triphenylphosphine and arsine. The very high heat of solution of triphenylphosphine in sulphuric acid and its resistance to sulphonation leave no doubt that it was sulphonated in the form of the triphenylphosphonium ion. A *meta*-orientation is thus highly probable.

Attempts to obtain the monosulphonated triphenylarsine by using concentrated sulphuric acid in place of SO_3–H_2SO_4 gave triphenylarsine oxide. Evidently the arsine is not sufficiently basic to be protected against oxidation by forming the arsonium salt but is first oxidised and then sulphonated (cf. ref. 22). The AsO group is *meta*-directing and so a *meta*-orientation of the trisulphonate is also highly probable.

We are indebted to Dr. L. A. Duncanson for an infrared investigation of the two sulphonic acids. The absorption bands in the appropriate region of the spectrum are listed in Table 3. Neither substance has bands in the 820 cm.$^{-1}$ region where *para*-substituted benzenes have strong bands, but both spectra are consistent with either *meta*- or *ortho*-orientations. To check that *para*-substituted arsines do have strong bands in the 820 cm.$^{-1}$ region a number were examined, as follows: (p-$Ph_2As{\cdot}C_6H_4{\cdot}SO_3)_2Ca$, 823 cm.$^{-1}$, p-$Ph_2As{\cdot}C_6H_4{\cdot}NH_2,HCl$, 819 cm.$^{-1}$, and p-$Ph_2As{\cdot}C_6H_4Br$, 814 cm.$^{-1}$. The sulphonated phosphine and trisulphonated arsine are certainly not *para*-derivatives, and all available evidence is strongly in favour of a *meta*-orientation for both acids.

TABLE 3. *Infrared spectra of sodium diphenylphosphinobenzene*-m-*sulphonate and the trisodium salt of tri-*(m-*sulphophenyl*)*arsine.*

$Ph_2P{\cdot}C_6H_4{\cdot}SO_3Na,2H_2O$ ...	794w	784 *	785m	772s	763s	752s	738s	723s	~690m
$As(m{\cdot}C_6H_4{\cdot}SO_3Na)_3$	799s	788s	753m	746s	738s	700 *	691s	673m	

* Shoulders.

Determination of Stability Constants.—These were determined by the titration method described in Part I. The method of calculating stability constants described there was also

[22] Michaelis, *Annalen*, 1902, **321**, 186.
[23] Chatt and Williams, *J.*, 1956, 3246.

used for the present amine systems. It could not be used for the phosphine and arsine because their affinities for silver ion are too high. In these circumstances [L] in all solutions, except where complex formation is almost complete, is so small compared with C_L, that all the C_L–C_M lines pass through the origin within experimental error (see Part I, Fig. 4). Then the intercepts which are necessary for determining the constants cannot be obtained. The method described in Part I can be used for the determination of all the constants β_1, β_2, etc., only when $\beta_1 < 1500$ l. mole^{-1}. When β_1 is higher, an alternative method must be used,[24] and since this has appeared only in Swedish we give the essentials of the method in an Appendix.

Experimental Technique.—[Ag^+] was measured by means of silver–silver halide electrodes as described in Part I. Chloride and bromide electrodes were used for the amine complexes and in the initial stages of a titration of silver solutions with the phosphine. Iodide electrodes were essential in the later stages of the phosphine measurements and were used throughout the arsine experiments. In the case of the phosphine even the iodide electrode was used to its limit, and an attempt to extend the range of measurements by using a pure silver electrode failed. The iodide electrodes were prepared analogously to Brown's chloride electrodes,[25] and were brownish-yellow. They were as good as the chloride and bromide electrodes when they were properly prepared but had a shorter life and tended to become erratic more easily. In the amine systems, and in the phosphine and arsine systems at lower ligand concentrations, the reproducibility of the e.m.f. was from 0·1 to 0·4 mv, but often in the latter systems E_M at high values of C_L could not be determined with better accuracy than ± 2 mv. Evidently the rate of the electrode reaction is slowed down very much when Ag^+ is strongly co-ordinated by the phosphine and arsine.

Systems Investigated.—Sodium sulphanilate was investigated at $I = 0{\cdot}1$M, to get constants under conditions directly comparable with those of the phosphine. The complexes were so weak, however, that a higher ionic strength $I = 1$M had to be used to cover a sufficient range of [L] to prove the existence of the third and fourth complexes, AgL_3 and AgL_4. This difference in ionic strength altered the constants very little (Tables 4 and 5). Titrations were also performed with buffer solutions, which besides sulphanilate of the concentration C_L' also contained sulphanilic acid of a concentration $= 1/5\ C_L'$. These buffer solutions gave the same results as the pure sulphanilate indicating that the silver salt had not been hydrolysed by the more basic sulphanilate solutions.

Sodium dimethylsulphanilate was investigated at $I = 0{\cdot}1$M. It forms weak complexes and only two were formed in appreciable amounts within the range of [L] used (Table 6). There was no sign of a stop at $\bar{n} = 2$ and our results do not preclude the existence of higher complexes in solutions of greater [L].

The acid dissociation constant was determined for comparison with those of sulphanilic and metanilic acids. Using the quinhydrone electrode at $I = 0{\cdot}1$M and 25° we obtained the value of $K_a = 4{\cdot}25 \times 10^{-4}$. This was corrected to $K_a = 2{\cdot}5 \times 10^{-4}$ at $I = 0$ and 25° by using the Debye–Hückel law.

Sodium metanilate was investigated only at $I = 1$M (Table 6) since the influence of ionic strength on the constants could be reasonably estimated from the sulphanilate measurement.

Sodium diphenylphosphinobenzene-*p*-sulphonate was investigated at $I = 0{\cdot}1$M because it is so sparingly soluble that the sodium-ion concentration had to be kept low. Nevertheless, since it forms strong complexes the whole range of complex formation could be followed up to a constant value of $\bar{n} = 3 = N$. The upper limit of [L] was not set by the low ionic strength but by the failure of the Ag–AgI electrodes. The sodium salt of the third complex $Na_2[Ag(Ph_2P{\cdot}C_6H_4{\cdot}SO_3)_3]$ was sparingly soluble and so complete titrations could be performed only when $C_M' \leqslant 5$ mM. When $C_L' = 10$ mM, this salt was precipitated as soon as C_L exceeded *ca.* 3 mM (Found: Ag, 8·7%. $C_{54}H_{42}O_9S_3P_3AgNa_2$ requires Ag, 9·21%). The titrations also had to be abandoned before the formation of complexes was complete when $C_M' = 1$ mM because the reproducibility of E_M was too poor at the higher values of C_L for such a low value of C_M'.

In spite of these limitations the silver complexes of the phosphine are so strong that the curves of C_A against E_M show a pronounced inflection when $C_L/C_M \approx 3$, indicating that complex formation is complete. Since [L] is significant compared with [ML_3] at this point, about 2% excess of the ligand over the three equivalents is necessary to reach the inflection point.

In Table 8, *C* the last two values of β_3 should be discarded as the Ag–AgI electrodes are

[24] Ref. 3, p. 21.
[25] Brown, *J. Amer. Chem. Soc.*, 1934, **56**, 646.

TABLE 4. *The system silver ion–sulphanilate ion* ($C_L' = 0{\cdot}1$M; $I = 0{\cdot}1$M).

A. E_M *as a function of* C_L.

$C_M' \longrightarrow$	10	2	$C_M' \longrightarrow$	10	2
C_L	E_M	E_M	C_L	E_M	E_M
1·32	0·5	0·5	16·7	5·9	6·1
2·60	1·0	1·0	21·1	7·2	7·6
3·85	1·4	1·5	25·0	8·6	9·2
5·07	1·8	1·9	28·6	9·9	10·5
6·26	2·0	2·1	34·8	11·9	12·5
9·09	3·3	3·5	40·0	13·8	14·5
11·8	4·0	4·3	50·0	18·8	19·8
14·3	4·9	5·2	62·5	21·4	23·0

B. Calculation of [L] *and derived stability constants.*

$C_M' \longrightarrow$	10	2	0				
E_M	C_L	C_L	$C_L = [L]$	X	X_1	X_2
2	5·8	5·5	5·5	1·081	14·7	
4	12·0	11·1	10·9	1·169	15·5	
6	17·9	16·7	16·4	1·263	16·0	
8	23·5	22·2	21·9	1·366	16·7	137
10	29·1	27·7	27·4	1·476	17·3	131
12	35·0	33·2	32·8	1·595	18·1	134
15	43·6	41·3	40·7	1·793	19·5	143
20	58·0	55·0	54·2	2·178	21·7	148

$\beta_1 = 13{\cdot}7 \pm 0{\cdot}8$ l. mole^{-1}. $K_1 = \beta_1$.
$\beta_2 = 120 \pm 20$ l.^{2} mole^{-2}. $K_2 = 9$ l. mole^{-1}.
$\beta_3 \simeq 500$ l.^{3} mole^{-3}.

TABLE 5. *The system silver ion–sulphanilate ion* ($C_L' = 1$M; $I = 1$M)

A. E_M *as a function of* C_L.

$C_M' \longrightarrow$	17·5	10	5	$C_M' \longrightarrow$	10	5
C_L	E_M	E_M	E_M	C_L	E_M	E_M
6·62	1·5	1·6	1·7	166·7	37·9	38·9
13·17	3·1	3·2	3·4	189·3	42·3	43·4
19·62	4·5	4·7	5·0	210·5	46·4	47·5
26·0	6·1	6·4	6·7	250	53·6	54·8
38·5	8·9	9·3	9·7	286	59·8	61·1
50·7	11·7	12·3	12·8	348	69·8	71·0
62·6	14·3	15·0	15·6	400	77·7	78·9
90·9	20·8	21·7	22·5	444	83·9	85·1
117·8		27·7	28·6	500	91·3	92·7
142·9		33·0	34·0			

B. Calculation of [L] *and derivation of the stability constants.*

$C_M' \longrightarrow$	17·5	10	5	0					
E_M	C_L	C_L	C_L	$C_L = [L]$	X	X_1	X_2	X_3	X_4
3	13·1	12·3	11·7	11·3	1·124	11·0			
5	21·7	20·5	19·4	18·6	1·215	11·6			
7	30·2	28·7	27·4	26·4	1·314	11·9			
10	43·3	41·2	39·8	38·4	1·476	12·4			
15	64·9	61·6	59·6	57·4	1·793	13·8	54		
20	87·3	83·4	80·7	78·1	2·178	15·1	56		
30		128·5	124·7	120·9	3·214	18·3	63	130	
40		177	173	169	4·745	22·3	69	130	
50		230	224	218	7·002	27·5	77	138	96
60		287	280	273	10·33	34·2	86	143	95
70		349	341	333	15·28	42·9	97	150	99
80		416	407	398	22·51	54·1	109	156	98
90		489	480	471	33·24	68·5	123	162	95

$\beta_1 = 10{\cdot}7 \pm 0{\cdot}8$ l. mole^{-1}. $K_1 = \beta_1$.
$\beta_2 = 47 \pm 5$ l.^{2} mole^{-2}. $K_2 = 4{\cdot}4$ l. mole^{-1}.
$\beta_3 = 120 \pm 20$ l.^{3} mole^{-3}. $K_3 = 2{\cdot}5$ l. mole^{-1}.
$\beta_4 = 100 \pm 30$ l.^{4} mole^{-4}. $K_4 = 0{\cdot}8$ l. mole^{-1}.

TABLE 6. *The system silver ion–*NN*-dimethylsulphanilate ion* ($C_L' = 0{\cdot}1$M; $I = 0{\cdot}1$M).

A. E_M *as a function of* C_L.

$C_M' \longrightarrow$	10	2	$C_M' \longrightarrow$	10	2
C_L	E_M	E_M	C_L	E_M	E_M
1·32	0·2	0·3	28·6	4·2	4·3
3·85	0·5	0·6	40·0	5·9	6·0
6·26	0·8	0·9	50·0	7·4	7·5
11·8	1·6	1·8	62·5	9·4	9·6
16·7	2·3	2·4	70·0	10·5	10·7
21·1	3·0	3·1			

B. Calculation of [L] *and derivation of the stability constants.*

$C_M' \longrightarrow$	10	2	0			
E_M	C_L	C_L	$C_L = [L]$	X	X_1	X_2
1	7·4	6·8	6·7	1·040	6·0	
2	14·4	13·7	13·5	1·081	6·0	
3	21·2	20·4	20·2	1·124	6·1	20
4	27·7	26·9	26·7	1·169	6·3	22
6	40·8	40·0	39·8	1·263	6·6	23
8	53·8	53·1	52·9	1·366	6·7	23
10	66·4	65·8	65·6	1·476	7·25	24

$\beta_1 = 5{\cdot}7 \pm 0{\cdot}3$ l. mole^{-1}. $K_1 = \beta_1$.
$\beta_2 = 23 \pm 5$ l.^{2} mole^{-2}. $K_2 = 4$ l. mole^{-1}.

beginning to fail. The mean of the remaining values is $\beta_3 = 3 \times 10^{-19}$ l.^{3} mole^{-3}. In this range of [L], where complex formation is complete, a value of $E_M = 600$ mv was chosen, corresponding to $X([L]_a) = 1{\cdot}39 \times 10^{10}$ and $[L]_a = 0{\cdot}77$ mM [(eqn. (1)]. These values were then used for the calculation of the constants β_1 and β_2 (Table 8, *D*). It is to be noted that the value of β_3 (Table 8, *C*) agrees well with that from the X functions at lower [L] (Table 8, *D*).

The trisodium salt of tri-(*m*-sulphophenyl)arsine was investigated at $I = 0{\cdot}2$M. In this case no precipitate was formed even when $C_M' = 15$ mM up to a ligand concentration of $C_L \approx 17$ mM. Higher values of C_L could not be used because the Ag–AgI electrodes failed, although no dissolution of halide took place (cf. p. 277). Thus when C_L was plotted against C_M, good straight lines were not obtained at the highest values of E_M; moreover the slopes of the lines, so

TABLE 7. *The system silver ion–metanilate ion* ($C_L' = 1$M; $I = 1$M).

A. E_M as a function of C_L.

C_M' ⟶	20	10	5	C_M' ⟶	20	10	5
C_L	E_M	E_M	E_M	C_L	E_M	E_M	E_M
13·16	4·3	5·0	5·3	285·7	75·1	78·1	79·2
38·47	12·5	14·1	15·0	318·2	81·2	84·0	85·0
62·5	19·9	22·3	23·5	347·9	86·3	88·9	90·0
117·6	36·3	39·7	40·7	400·0	94·8	97·1	98·3
166·6	49·1	52·5	53·7	444·4	101·2	103·6	104·8
210·5	59·5	62·7	63·9	500	109·4	111·2	112·4
250·0	68·0	71·0	72·2				

B. Calculation of [L] *and derivation of the stability constants.*

C_M' ⟶ 20	10	5	0					
E_M	C_L	C_L	C_L	$C_L = [L]$	X	X_1	X_2	X_3	X_4
3	9·2	8·0	7·2	6·6	1·124	18·8			
5	15·2	13·2	12·4	11·6	1·215	18·5	129		
7	21·3	18·8	17·6	16·4	1·314	19·1	128		
10	30·6	27·0	25·3	23·6	1·476	20·2	136		
15	46·4	41·0	38·5	35·9	1·793	22·1	142		
20	62·6	55·6	52·4	49·0	2·178	24·0	143		
30	96·0	86·4	82·8	79·0	3·214	28·0	139		
40	132	119	115	110	4·745	34·0	155	227	245
50	170	157	152	146	7·002	41·1	165	240	274
60	212	199	193	187	10·33	49·9	176	246	245
70	260	245	239	232	15·28	61·6	192	267	289
80	311	296	290	283	22·51	76·0	208	276	269
90	370	355	348	340	33·24	94·8	229	291	268
100	435	420	411	403	49·20	119·6	255	310	273
110	505	490	482	474	72·45	150·7	282	321	255

$\beta_1 = 17 \pm 2$ l. mole^{-1}. $K_1 = \beta_1$.
$\beta_2 = 130 \pm 20$ l.^{2} mole^{-2}. $K_2 = 8$ l. mole^{-1}.
$\beta_3 = 200 \pm 30$ l.^{3} mole^{-3}. $K_3 = 1{\cdot}5$ l. mole^{-1}.
$\beta_4 = 250 \pm 50$ l.^{4} mole^{-4}. $K_4 = 1{\cdot}3$ l. mole^{-1}.

far as they could be determined, tended to decrease with increasing E_M. However, a constant value of $\bar{n} = 1$ had been reached at lower values of E_M. This indicates almost complete formation of the first complex and values of $X_1 = \beta_1$ calculated from [L], found as intercepts, are fairly constant (Table 9, *B*). As the upper values of β_1 were suspect the mean was not taken in this case, but a value of $X([L]_a) = 507{\cdot}0$, corresponding to $E_M = 160$ mv was chosen as the upper limit of integration of eqn. (3). This value was chosen because the corresponding value of $[L]_a$ was obtained as the intercept of a good straight C_L–C_M line; also the intercept was sufficiently large to be determined fairly accurately. The values of X_1 resulting from the integration are in the last column of Table 9, *B*. The constancy is good and also the agreement with the values found from the intercepts. The mean value of X_1 may therefore be taken as an accurate value of β_1.

APPENDIX

Fronaeus's Method for the Determination of Stability Constants when β_1 is Greater than or Equal to 1500 l. mole^{-1}.—The notation is defined in the Appendix to Part I (preceding paper). This method by which β_1, β_2 etc. are determined (p. 274) uses the fact that the

TABLE 8. *The system silver ion–diphenylphosphinobenzene-*p*-sulphonate ion* ($C_L' = 0{\cdot}03$M; $I = 0{\cdot}1$M).

A. E_M as a function of C_L.

$C_M' \longrightarrow$	10	5	2	1	C_M'	5	2
C_L	E_M	E_M	E_M	E_M	C_L	E_M	E_M
0·199	—	1·0	2·7	6·0	5·27	—	512
0·395	1·2	2·2	5·7	13·4	5·41	—	551
0·588	—	—	9·1	23·5	5·67	117·6	585
0·779	2·4	4·6	13·1	40·4	6·32	136·4	623
0·968	—	—	17·6	71·7	6·68	—	633
1·154	3·5	7·2	23·2	108·0	7·50	172·5	644
1·338	—	—	—	129·3	8·57	216·5	
1·52	4·8	10·0	38·7	145·7	9·08	248	
1·875	6·1	13·1	69·8	173·8	9·55	294	
2·22	—	16·8	105·8	210·5	9·83	338	
2·39	—	—	—	235·9	10·00	382	
2·725		23·4	132·3		10·18	450	
3·22		—	154·6		10·26	482	
3·53		39·3	170·8		10·35	510	
3·99		—	199·3		10·43	534	
4·28		69·0	224·5		10·61	566	
4·72		—	282·6		10·86	592	
5·00		97·8	366		11·25	616	
5·13		—	445		12·00	638	

B. Determination of $\bar{n}$ over the whole range of complex formation.

$C_M' \longrightarrow$	10	5	2	1	
E_M	C_L	C_L	C_L	C_L	$\bar{n}$
2	0·67	0·36	0·16	—	0·068
5	1·58	0·83	0·35	0·17	0·168
10	2·86	1·52	0·63	0·31	0·318
15	3·86	2·05	0·87	0·43	0·443
20	4·67	2·48	1·04	0·53	0·550
30		3·12	1·34	0·68	0·695
40		3·55	1·53	0·78	0·805
70		4·31	1·88	0·97	1·00
100		5·05	2·15	1·09	1·15
125		5·92	2·58	1·31	1·45
150		6·77	3·12	1·60	1·74
175		7·56	3·61	1·89	1·98
200		8·23	4·00	2·14	2·22
230		8·82	4·36	2·35	2·42
280		9·44	4·71		2·68
350		9·87	4·93		2·89
450		10·18	5·14		3·00

C. Determination of β_2 from solutions of high C_L where complex formation is complete.

$C_M' \longrightarrow$	5	2				
E_M	C_L	C_L	$C_L = [L]$	$\bar{n}$	X	$10^{-19}\beta_2$
500	10·31	5·25	0·24	3·03	$2{\cdot}85 \times 10^8$	2·1
550	10·50	5·42	0·39	3·1	$2{\cdot}0 \times 10^9$	3·3
580	10·72	5·62	0·56	3·2	$6{\cdot}5 \times 10^9$	3·7
600	10·96	5·86	0·80	3·2	$1{\cdot}4 \times 10^{10}$	3·2
620	11·33	6·27	1·25	3·1	$3{\cdot}1 \times 10^{10}$	(1·6)
640	12·10	7·20	2·35	3·1	$6{\cdot}8 \times 10^{10}$	(0·52)

D. Calculation of [L] and derivation of β_1 and β_2.

E_M	$\bar{n}$	$\log [L]_a/[L]$	[L]	X	$10^{-6}X_1$	$10^{-14}X_2$	$10^{-19}X_3$
2	0·068	6·154	$0{\cdot}54 \times 10^{-6}$	1·081	1·5		
5	0·168	5·704	$1{\cdot}52 \times 10^{-6}$	1·215	1·43		
10	0·318	5·344	$3{\cdot}48 \times 10^{-6}$	1·476	1·37		
15	0·443	5·120	$5{\cdot}83 \times 10^{-6}$	1·793	1·36		
20	0·550	4·950	$8{\cdot}63 \times 10^{-6}$	2·178	1·37		
30	0·695	4·678	$1{\cdot}61 \times 10^{-5}$	3·214	1·37		
40	0·805	4·460	$2{\cdot}67 \times 10^{-5}$	4·745	1·40		
70	1·00	3·904	$9{\cdot}6 \times 10^{-5}$	15·28	1·49	1·25	
100	1·15	3·428	$2{\cdot}87 \times 10^{-4}$	49·04	1·68	1·08	
125	1·45	3·096	$6{\cdot}17 \times 10^{-4}$	129·7	2·08	1·15	
150	1·74	2·832	$1{\cdot}13 \times 10^{-3}$	343·5	3·03	1·47	2·4
175	1·98	2·604	$1{\cdot}91 \times 10^{-3}$	908	4·75	1·77	3·0
200	2·22	2·404	$3{\cdot}04 \times 10^{-3}$	2405	7·92	2·16	3·2
230	2·42	2·186	$5{\cdot}01 \times 10^{-3}$	7730	15·4	2·80	3·2
280	2·68	1·852	0·0108	54,100	50·2	4·52	3·1
350	2·89	1·432	0·0285	$8{\cdot}26 \times 10^5$	290	10·15	3·1
450	3·00	0·846	0·1096	$4{\cdot}04 \times 10^7$	3690	33·7	3·0
500	3·0	0·564	0·210	$2{\cdot}83 \times 10^8$	13,500	64·3	3·0
600	3	0	$[L]_a = 0{\cdot}77$	$X([L]_a) = 1{\cdot}39 \times 10^{10}$			

$\beta_1 = 1{\cdot}4 \pm 0{\cdot}2 \times 10^6$ l. mole^{-1}. $K_1 = \beta_1$.
$\beta_2 = 1{\cdot}2 \pm 0{\cdot}2 \times 10^{14}$ l.^{2} mole^{-2}. $K_2 = 0{\cdot}9 \times 10^8$ l. mole^{-1}.
$\beta_3 = 3 \pm 0{\cdot}5 \times 10^{19}$ l.^{3} mole^{-3}. $K_3 = 2{\cdot}5 \times 10^5$ l. mole^{-1}.

slopes of the C_L–C_M lines, which are equal to the ligand number $\bar{n}$, can be determined more accurately when the complexes formed are strong than when they are weak. This arises because the family of curves of C_L against E_M at constant C_M (see Part I, Fig. 3) is better spaced. Also, when strong complexes are formed, $\bar{n}$ will usually reach its maximum value N within the range of [L] available. Hence at a sufficiently high [L] the C_L–C_M

TABLE 9. *The system silver ion–trianion of tri-*(m-*sulphophenyl*)*arsine* ($C_L' = 0{\cdot}0333$M; $I = 0{\cdot}2$M).

A. E_M *as a function of* C_L.

$C_M' \longrightarrow$	15	10	5	2	$C_M' \longrightarrow$	15	10	5	2
C_L	E_M	E_M	E_M	E_M	C_L	E_M	E_M	E_M	E_M
0·44	0·9	1·3	2·7	6·8	7·55	—	88·5	—	—
0·87	1·8	2·8	5·7	15·4	7·82	—	109·1	—	—
1·28	2·6	4·1	8·8	28·8	8·07	—	124·4	—	—
1·69	—	5·6	12·6	55·7	8·33	37·3	135·0	179·0	191·3
2·08	4·5	7·0	16·8	101·3	8·93	46·5	151·4	—	—
2·47	—	8·6	21·8	125·0	9·51	59·9	161·4	186·4	197·0
2·84	—	10·4	28·0	137·7	10·07	85·1	—	—	—
3·03	7·1	—	31·9	142·2	10·60	122·5	174·1	192·0	201·3
3·21	—	12·2	36·2	145·9	11·10	143·6	—	—	—
3·57	—	14·1	48·1	152·3	11·58	155·4	182·4	196·5	205·1
3·74	—	—	57·3	—	12·49	169·7	188·5	200·1	—
3·92	9·9	16·3	65·9	157·5	13·32	178·8	193·3	203·4	211·4
4·26	—	—	96·5	—	14·09	185·4	—	206·1	—
4·76	12·9	22·3	127	166·8	14·80	190·4	200·6	208·6	216·2
5·55	16·4	29·7	148·8	174·2	15·46	194·6	—	210·8	—
6·30	20·3	40·7	—	—	16·08	198·0	—	212·8	—
7·01	25·0	58·8	168·0	184·1	16·65	200·9	208·1	214·5	222·1
7·28	—	70·9	—	—					

B. Calculation of [L] *and derivation of* β_1.

$C_M' \longrightarrow$	15	10	5	2	0							
E_M	C_L	C_L	C_L	C_L	$C_L = [L]$	X'	$10^{-5}X_1$ *	$\bar{n}$	$\log \frac{[L]_o}{[L]}$	[L]	$10^{-5}X_1$ †
1	0·50	0·33	0·16	0·08		1·040		0·034	4·3039	$1{\cdot}20 \cdot 10^{-4}$	(3·3)
2	1·00	0·65	0·32	0·16		1·081		0·068	3·9519	$2{\cdot}70 \cdot 10^{-4}$	(3·0)
3	1·44	0·96	0·48	0·22		1·124		0·100			
4	1·88	1·24	0·62	0·28		1·165		0·131	3·5960	$6{\cdot}13 \cdot 10^{-4}$	2·7
6	2·62	1·80	0·91	0·40		1·263		0·190			
8	3·32	2·32	1·18	0·51		1·365		0·249			
10	3·95	2·76	1·41	0·61		1·476		0·299	3·1050	$1{\cdot}90 \cdot 10^{-3}$	2·51
15	5·24	3·71	1·92	0·85		1·792		0·416			
20	6·25	4·46	2·34	1·03		2·178		0·514	2·6786	$5{\cdot}07 \cdot 10^{-3}$	2·32
30	7·60	5·58	2·94	1·31		3·215		0·665	2·3831	$1{\cdot}00 \cdot 10^{-2}$	2·22
40	8·51	6·26	3·34	1·54		4·744		0·768	2·1483	$1{\cdot}72 \cdot 10^{-2}$	2·18
50	9·10	6·72	3·61	1·64		7·003		0·838			
60	9·50	7·05	3·80	1·75		10·34		0·888	1·7431	$4{\cdot}37 \cdot 10^{-2}$	2·14
80	9·98	7·42	4·08	1·90		22·52		0·934			
100	10·26	7·72	4·30	2·07		49·04		0·959	1·0387	$2{\cdot}21 \cdot 10^{-1}$	2·17
120	10·55	7·97	4·59	2·38	0·60	106·8	(1·75)	0·975	0·6899	$4{\cdot}94 \cdot 10^{-1}$	2·14
140	11·01	8·49	5·10	2·92	1·15	232·7	2·02	0·981	0·3446	1·094	2·12
160	11·85	9·40	6·33	4·10	2·41	507·0	2·10	0·980	0	$2{\cdot}41 = [L]_o$	2·10
170	12·52	10·22	7·20	5·05	3·40	748·1	2·20	0·983			
180	13·44	11·21	8·48	6·37	4·90	1104	2·25	0·983			
190	14·69	12·72	10·18	8·02	7·05	1630	2·31	—			
200	16·45	14·65	12·41	10·21	9·60	2405	2·50	—			
210	—	17·2	15·21	12·92	12·70	3550	(2·80)	—			

$\beta_1 = K_1 = 2{\cdot}3 \pm 0{\cdot}3 \times 10^5$ l. mole^{-1}.

* Calculated from values of [L] found by extrapolation to $C_M = 0$.
† Calculated from values of [L] found from eqn. (3).

lines at constant E_M (see Part I, Fig. 4) will run parallel, with their slopes equal to N, which can thus be determined.

As C_L increases and complex formation approaches completion, *i.e.*, $\bar{n} \longrightarrow N$, [L] will sooner or later become comparable in magnitude to C_L. It will then be possible again to determine [L] from the intercept of the C_L–C_M curves. In the case of extremely strong complexes such as those formed by the phosphine, this happens only when $C_L > N \times C_M$. In such solutions the highest complex ML_N is completely dominating and $C_M = [ML_N]$. The function X, which is directly calculated from E_M [see Part I, eqns. (1), (2), and (7)], can then be simplified to

$$X = \beta_N[L]^N \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where corresponding values of X and [L] and the constant N are known, and hence β_N.

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In order to find the lower constants β_1, β_2, etc., eqn. (10) of Part I is transformed to give eqn. (2):

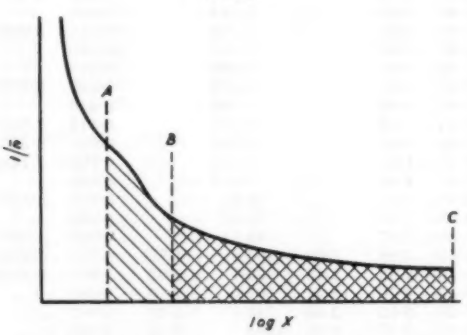
$$\bar{n} = \frac{\sum_{n=1}^{N} n\beta_n[L]^n}{X} = \frac{[L]\frac{dX}{d[L]}}{X} = \frac{dX}{X}\Big/\frac{d[L]}{[L]} = \frac{d \log X}{d \log [L]} \quad . \quad . \quad . \quad (2)$$

On integration this gives eqn. (3):

$$\log \frac{[L]_a}{[L]_j} = \int_{X([L]_j)}^{X([L]_a)} \frac{1}{\bar{n}} d \log X \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

If the corresponding values $[L]_a$ and $X([L]_a)$ are chosen within a range where $[L]_a$ can be determined as the intercept of a C_L–C_M line, it is possible to find the value of $[L]_j$ corresponding to any chosen value $X([L]_j)$ by evaluating the integral of eqn. (3). This is conveniently done graphically by plotting $1/\bar{n}$ as a function of log X to give a curve as shown in Fig. 3, and measuring the areas under the curve from a fixed limit, log $X([L]_a)$ (*A* in Fig. 3), to various lower limits, log $X([L]_j)$ (*B*, *C* in Fig. 3). Corresponding values of X and $[L]_j$ are thus obtained over the whole range of complex formation and the stability constants of the lower complexes are calculated as usual [Part I, eqns. (3) and (4)]. The best values of $[L]_a$ and $X([L]_a)$ to serve as the fixed upper limit can be obtained from the value of β_N found above. In the range of [L] (or E_M) where the relation $X = \beta_N[L]^N$ holds, a value of E_M is chosen and corresponding values of $X([L]_a)$ and $[L]_a$ are calculated.

FIG. 3.



If polynuclear complexes exist the slopes of the C_L–C_M lines are no longer equal to $\bar{n}$ but to a quantity less than $\bar{n}$. The above method therefore presumes that polynuclear complexes are not formed. This is not easy to prove experimentally, but an indication can be obtained by the method described in Part I over the range where [L] can be determined by the intercept method. Even if no polynuclear complexes are formed in this range of high [L] it cannot be assumed that they are not formed at lower values of [L] and our main arguments for supposing that they are not formed in our phosphine and arsine systems are (i) that there is only one strong donor atom in each ligand molecule and (ii) that the analogous sulphides and selenide were shown experimentally not to give polynuclear complexes although they were in equilibrium with a much higher $[Ag^+]$ at low [L] than the phosphine and the arsine.

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56. *Nuclear Resonance Spectra of Some Peroxy-salts.*

By T. M. Connor and R. E. Richards.

Proton resonance spectra have been recorded at 90° K of crystalline perborates of sodium, potassium, and rubidium, three sodium perpyrophosphates, and sodium percarbonate. The perborates contain most of their hydrogen as water of crystallisation; the small amounts of hydrogen peroxide of crystallisation are not enough to account for all the active oxygen present. They are therefore probably true peroxy-salts. The perpyrophosphates and sodium percarbonate give narrow proton resonance lines, which are consistent with the view that all the hydrogen is present as hydrogen peroxide of crystallisation. These are therefore probably not true peroxy-salts.

When certain borates, carbonates, or pyrophosphates are treated with hydrogen peroxide under appropriate conditions, solids which contain active oxygen can be crystallised from the solutions. This active oxygen has the oxidising properties of hydrogen peroxide.

The perborates and percarbonates have a somewhat variable composition; their stoicheiometry depends rather critically on the conditions of preparation. The formulæ and structures of these compounds have been studied by Partington and Fathallah[1] and others,[2] but there does not appear to be any conclusive evidence which shows whether they contain true peroxyanions or whether their active oxygen is present merely as hydrogen peroxide of crystallisation.

Proton resonance spectra of these compounds were measured in order to determine whether or not hydrogen is present as water or hydrogen peroxide of crystallisation. The absorption curves at low temperatures are very much broader if the protons are in water molecules than if they are in molecules of hydrogen peroxide.

Experimental

Perborates.—Preparation. Sodium, potassium, rubidium, and cæsium perborates were prepared by Partington and Fathallah's method.[1] A concentrated solution of the alkali-metal metaborate was added to 30% hydrogen peroxide, and the mixture cooled to −10°. After about 15 min. the perborate crystals were removed and dried.

Analysis. The alkali metal was estimated[3] by titration with 0·1N-sulphuric acid with bromophenol-blue as indicator. This amount of standard acid was then added to another portion of the solution and the concentration of BO_2^- found by titration with 0·1N-sodium hydroxide in the presence of mannitol, with phenolphthalein. The active oxygen (O_a) was determined by titration with potassium permanganate solution.

Sodium perborate. The crystals were dried in a vacuum-desiccator for 16 hr. (P_2O_5) (Found: Na^+, $1{\cdot}00_0$; BO_2^-, $1{\cdot}00_0$; O_a, $1{\cdot}92_3$; H_2O, $1{\cdot}57_6$). The compound approximates to the formula $NaBO_4,\frac{3}{2}H_2O$.

Potassium perborate. The potassium metaborate was prepared from potassium hydroxide and boric acid[4] (Found for the perborate: K^+, $1{\cdot}00_0$; BO_2^-, $1{\cdot}00_0$; O_a, $1{\cdot}73_6$; H_2O, $0{\cdot}67_3$).

Rubidium perborate. Rubidium nitrate was mixed with 2 equiv. of oxalic acid, and the mixture moistened with water and heated gently in a platinum crucible until no more nitrous fumes came off. The residue was converted into the carbonate at 800° in an electric furnace. 1 Equiv. of boric acid was added and the mixture heated to give a clear melt. The cold product was extracted with enough water to give a 50% solution of rubidium metaborate, and the perborate prepared therefrom (Found: Rb^+, 1·00; BO_2^-, 1·00; O_a, 1·90; H_2O, 0·70).

[1] Partington and Fathallah, *J.*, 1949, 3421.
[2] Menzel, *Z. anorg. Chem.*, 1927, **167**, 193; Bosshard and Zwicky, *Z. angew. Chem.*, 1912, **25**, 938, 993; Carpeni, *Bull. Soc. chim. France*, 1949, 742; Tanata, *Z. phys. Chem.*, 1898, **26**, 132; Bruhat and Dubois, *Compt. rend.*, 1905, **140**, 506.
[3] Menzel, *Z. anorg. Chem.*, 1927, **164**, 1.
[4] Dulesky, *Z. anorg. Chem.*, 1906, **50**, 38.

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Sodium perborate tetrahydrate. This was supplied and analysed by Laporte Chemicals Ltd. (Found: Na, 1·00; BO_2^-, 1·00; O_a, 0·94; H_2O, 3·63).

Sodium Perpyrophosphate.—Three samples were supplied and analysed by Laporte Chemicals Ltd. They were $Na_4P_2O_7,H_2O_2$ (Found: O_a, 5·92; P_2O_5, 46·2%), $Na_4P_2O_7,2H_2O_2$ (Found: O_a, 10·39; P_2O_5, 41·7%), and $Na_4P_2O_7,3H_2O_2$ (Found: O_a, 12·93; P_2O_5, 40·8%).

The active oxygen being assumed to be present as H_2O_2 and the P_2O_5 as $Na_4P_2O_7$, the total contents of these samples are then 99·1%, 100·2%, and 103·9% respectively.

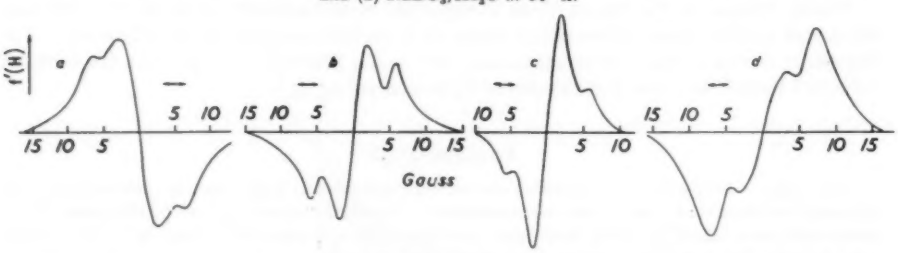
Sodium Percarbonate.—This was supplied and analysed by Laporte Chemicals Ltd. The analysis [Found: Na_2CO_3, 63·7; O_a, 13·0; H_2O (by difference), 23·3%] corresponds approximately to $Na_2CO_4,2H_2O$, although the compound is usually said to be $2Na_2CO_3,3H_2O_2$.

Nuclear Resonance Measurements.—The recording nuclear magnetic resonance spectrometer described previously [5] was used. The amplitude of the radiofrequency field was chosen to be well below the value at which saturation becomes apparent. The spectrometer records the first derivative of the nuclear resonance absorption curve.

Results and Discussion

Perborates.—The differentials of the absorption curves of proton resonances are shown in Fig. 1. The peak-to-peak amplitude of the modulation field is shown by the double ended arrows. Each curve appears to be a superposition of a broad and a narrower line. The numerical results are summarised in the Table, in which the second moments given have been corrected for the effect of modulation and field inhomogeneity.[6]

Fig. 1. *Derivative of proton resonance of* (*a*) $NaBO_4,\frac{3}{4}H_2O$; (*b*) $KBO_4,\frac{1}{2}H_2O$; (*c*) $RbBO_4,\frac{1}{2}H_2O$; *and* (*d*) $NaBO_3,4H_2O$ *at* 90° K.



The hydrogen atoms of water molecules are about 1·6 Å apart, and crystalline hydrates give a proton resonance spectrum characteristic of these relatively closely spaced pairs of protons. The absorption curve is a broad doublet with a shallow central minimum.[7] The derivative of the absorption curve, which is usually recorded experimentally, has two outer peaks separated by about 12 gauss.

Compound	Temp. (° K)	Second moment (gauss²)	No. of measurements	Derivative curve Separation (gauss) of inner maxima	outer maxima	Ratio of areas of broad to narrow absorption lines
$NaBO_4,\frac{3}{4}H_2O$						
Sodium perborate ...	90	20·7 ± 1	7	5·3	12·0	4·5
$KBO_4,\frac{1}{2}H_2O$						
Potassium perborate	90	19·7 ± 0·8	4	4·1	11·9	4
$RbBO_4,\frac{1}{2}H_2O$						
Rubidium perborate	20	8·9 ± 0·4	9	3·5	11·4	—
$RbBO_4,\frac{1}{2}H_2O$						
Rubidium perborate	90	Approximately the same as at 20° K				
$NaBO_3,4H_2O$						
Sodium perborate tetrahydrate	90	29·5 ± 1	3	6·2	15·5	10

[5] Richards and Smith, *Trans. Faraday Soc.*, 1951, **47**, 1261; Pratt and Richards, *ibid.*, 1953, **49**, 744.

[6] Andrew, *Phys. Rev.*, 1953, **91**, 425.

[7] Pake, *J. Chem. Phys.*, 1948, **16**, 327.

If the hydrogen atoms in these salts are present either in H–O–O–H molecules or as OH groups, the protons are more widely separated than in a water molecule, and a much narrower proton resonance curve would be obtained.

The derivative curves of the sodium and potassium perborates show a double set of maxima. The outer maxima are separated by about 12 gauss, the separation found in hydrates. It seems reasonable, therefore, to attribute these outer maxima to the presence of water molecules in the crystal lattice, and the inner maxima to protons in OH or HO_2H groups. The relative numbers of protons in the H_2O and OH groups can be estimated by decomposing the observed derivative curve into its two components and comparing the intensities of the corresponding absorption curves. This can be done by superimposing the derivative curve normally obtained from a crystalline salt hydrate [7] on the experimental curve; the narrower line is then obtained by subtraction. This procedure is illustrated in Fig. 2, of which the continuous line is half the experimentally observed derivative curve of sodium perborate tetrahydrate. The broken lines show how the continuous curve can be resolved into the broad (*a*) and the narrow (*b*) component. The two components of the resolved derivative curve can be integrated separately and give the

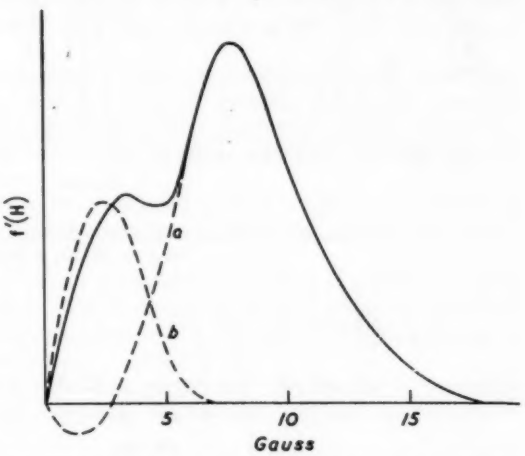
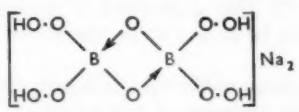
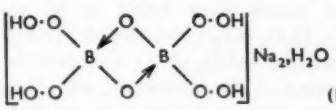


FIG. 2. *Resolution of half the derivative curve of* $NaBO_3,4H_2O$ *into two components* (90° K).

absorption curves shown in Fig. 3 for $NaBO_4,\frac{3}{2}H_2O$. The relative areas of these two curves give the approximate ratio of the number of protons in the two situations. In this case the area under the broad doublet is 4·5 times that under the narrower curve.

Partington and Fathallah [1] obtained a compound approximating to $NaBO_4,H_2O$ by drying the above perborate *in vacuo* (P_2O_5) and attributed to it the structure (I), so that by analogy the structure of $NaBO_4,\frac{3}{2}H_2O$ would be (II). If this formula is correct, then the ratio of the number of doublet protons to that of Q " singlet " protons = 2/4 = 0·5.

(I) 



(II)

However, the above results indicate that this ratio is about 4·5, and are therefore inconsistent with this formula. Most of the protons are present in the form of pairs in water molecules and the small number of singlet protons is not sufficient to account for all the active oxygen present as hydrogen peroxide of crystallisation. This compound is, therefore, probably a true hydrate of a peroxy-salt which contains some hydrogen peroxide of crystallisation.

Potassium perborate. $KBO_4,\frac{1}{2}H_2O$. The derivative curve was resolved into two components as in the case of the sodium compound, and the areas of the integrated components compared (Fig. 3*b*). The doublet : singlet ratio was 4. It is, therefore, probable that this compound is a true peroxy-salt with the hydrogen atoms present as water molecules, but with some hydrogen peroxide of crystallisation.

Rubidium perborate. $RuBO_4,\frac{1}{2}H_2O$. The protons in this sample were very readily saturated and the signals were rather weak. It is clear, however, that the derivative curve is much narrower than in the above salts, and the shape of the outer portions of the curve did not correspond closely to that usually observed with hydrates. This might be due to reorientation of the water molecules in the crystal lattice (although the curve

FIG. 3. *Two components of the absorption curve of proton resonance of* (*a*) $NaBO_4,\frac{3}{2}H_2O$, (*b*) $KBO_4,\frac{1}{2}H_2O$, *and* (*c*) $NaBO_3,4H_2O$ *at* 90° K.

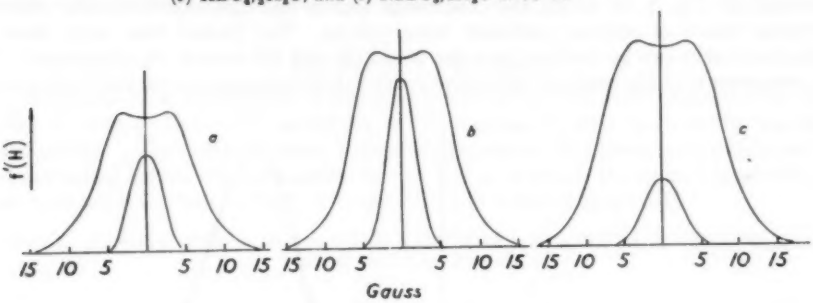
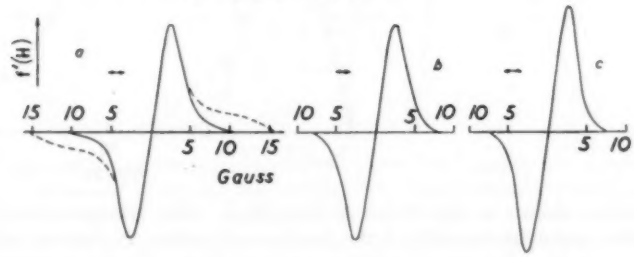


FIG. 4. *Derivative of proton resonance of* (*a*) $Na_4P_2O_7,H_2O_2$, (*b*) $Na_4P_2O_7,2H_2O_2$, *and* (*c*) $Na_4P_2O_7,3H_2O_2$ *at* 90° K.



was not significantly changed on cooling from 90° K to 20° K) or to the absence of water molecules. The signals were not good enough to warrant a more detailed discussion.

Sodium perborate tetrahydrate. The derivative curve was resolved into two components (Fig. 2) and after integrating these (Fig. 3*c*), the relative areas of the doublet and singlet curves were found to be about 10 : 1. If this compound is formulated as $NaBO_2,H_2O_2,3H_2O$, the doublet : singlet ratio would be 3, and so on the above evidence the formula $NaBO_3,4H_2O$ is preferable.

General.—The perborates, with the possible exception of the rubidium salt, give proton resonance spectra which indicate that they are true hydrates of peroxy-salts. They all appear to contain hydrogen peroxide of crystallisation, but not enough to account for the total active oxygen found. The difficulty of obtaining pure salts with accurate analyses may be associated with the instability of the peroxyanion and the ability of hydrogen peroxide to replace water of crystallisation.

The Perpyrophosphates.—Sodium perpyrophosphate I, $Na_4P_2O_7,H_2O_2$. The first measurements on this sample gave derivative curves with long tails (Fig. 4*a*, broken curve).

It was suspected that these tails might arise from the broad contribution of the protons in moisture, so the sample was dried *in vacuo* (P_2O_5) for 3 days. The broad edges of the derivative curve were no longer observed, and the final result is shown in Fig. 4*a* (continuous curve). The second moment was $6{\cdot}3 \pm 0{\cdot}5$ gauss^2 (9 measurements), and the line width was 5·33 gauss.

Sodium perpyrophosphate II, $Na_4P_2O_7,2H_2O_2$. The derivative curve obtained is shown in Fig. 4*b*. The second moment was $5{\cdot}5 \pm 0{\cdot}3$ gauss^2 (8 measurements) and the line width 5·40 gauss.

Sodium perpyrophosphate III, $Na_4P_2O_7,3H_2O_2$. The derivative curve is shown in Fig. 4*c*; the second moment was $4{\cdot}1 \pm 0{\cdot}2$ gauss^2, and the line width 5·30 gauss.

The derivative curves of these samples are all very similar. The line widths are the same and the curves differ only slightly near the outer edges. These differences might be due to small amounts of water which could not be removed. Sodium perpyrophosphate I could be written either as $Na_4P_2O_8,H_2O$ or as $Na_4P_2O_7,H_2O_2$. The absence of the broad line characteristic of water of crystallisation suggests that the first formula is incorrect and that the active oxygen is present as hydrogen peroxide of crystallisation, which gives a narrow proton resonance line. The close similarity of the proton resonances in the other two salts suggests that they too consist of sodium pyrophosphate with molecules of hydrogen peroxide of crystallisation.

It was found that the active oxygen in these compounds could be extracted with ether, even when it had been dried with lithium hydride, and the presence of hydrogen peroxide in the ether was demonstrated by the addition of sodium dichromate solution, when the characteristic blue colour developed. Only small amounts of the active oxygen of the perborates could be extracted with ether.

Sodium Percarbonate.—The derivative curve obtained at 90° K is narrow and similar in appearance to those of Fig. 4. The second moment was $4{\cdot}0 \pm 0{\cdot}2$ gauss^2 (6 measurements) and the line width was 5·33 gauss.

The compound clearly does not contain an appreciable proportion of protons as water molecules since the resonance is narrow. The composition $Na_2CO_4,2H_2O$ is, therefore, probably incorrect. The formula usually assigned to this compound, $2Na_2CO_3,3H_2O_2$, is consistent with the narrow nuclear resonance line obtained.

Conclusion.—The perborates appear to be true peroxy-salts with water of crystallisation. They all contain some hydrogen peroxide of crystallisation but not enough to account for all the active oxygen.

The perpyrophosphates and percarbonates studied do not contain appreciable amounts of water of crystallisation, and the hydrogen is present as hydrogen peroxide of crystallisation.

We thank the Hydrocarbon Research Group of the Institute of Petroleum for financial help. We are grateful to Laporte Chemicals Ltd. for some samples.

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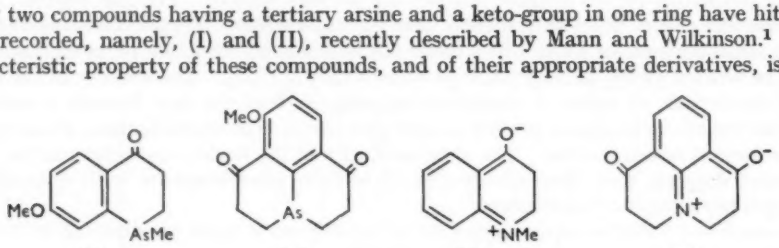
XUM

57. *The Synthesis and Structure of* 10-*Phenylarsacridone.*

By Emrys R. H. Jones and Frederick G. Mann.

This arsacridone is the third example of a cyclic system having a keto- and a tertiary arsine group in one ring. The two previous examples, and their appropriate derivatives, showed very little evidence for charge separation within the molecule, whereby the arsenic atom would have become 4-covalent. In the arsacridone derivative, there is considerable chemical and physical evidence that this charge separation makes a substantial contribution to the structure.

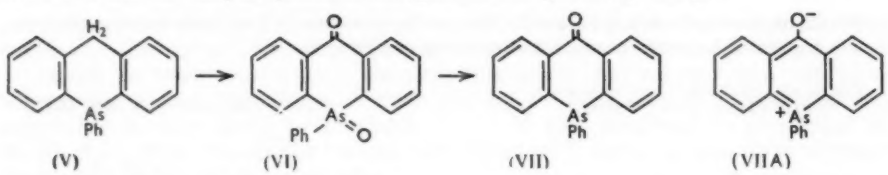
Only two compounds having a tertiary arsine and a keto-group in one ring have hitherto been recorded, namely, (I) and (II), recently described by Mann and Wilkinson.[1] One characteristic property of these compounds, and of their appropriate derivatives, is that



(I) (II) (III) (IV)

internal charge separation, whereby the arsenic atom would become 4-covalent, is virtually non-existent, and they are thus in marked contrast to their nitrogen analogues which provide strong evidence for such separation. For example, the arsinoline (I) is a colourless solid, but 1 : 2 : 3 : 4-tetrahydro-1-methyl-4-oxoquinoline is a yellow liquid,[2] the colour being undoubtedly caused by a marked contribution by the polar form (III): this colour is associated in the ultraviolet spectrum with a broad band at 384 mμ, which is absent in that of the arsinoline (I). Similarly, the arsulolidine (II) and 1 : 6-dioxojulolidine[3] form colourless and bright yellow crystals respectively, the colour of the latter being caused by contributions of the two polar forms of type (IV). (Strict comparison of the two series is not possible because of the presence of the methoxyl group in the arsenic compounds but it is probable that this group has little effect in this respect.[1])

There is a similar contrast between the colourless 1 : 2-dihydro-1-methoxy-1-methylquinolino(3′ : 2′-3 : 4)arsinoline, which gives a pale yellow hydrochloride, and the yellow 1 : 2-dihydro-1-methylquinolino(3′ : 2′-3 : 4)quinoline, which forms a monohydrochloride[5] whose purple colour is undoubtedly determined by a considerable contribution from the form in which the dihydroquinolino-nitrogen atom is positively charged.



(V) (VI) (VII) (VIIA)

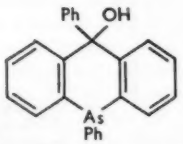
We have therefore selected for study 10-phenylarsacridone (VII), for this ring system, by analogy with that of the markedly inert yellow 10-phenylacridone, appeared to offer a high chance of showing charge separation, as in (VIIA), with consequent considerable deactivation of both the arsine and the carbonyl group.

[1] Mann and Wilkinson, *J.*, 1957, 3336.
[2] Allison, Braunholtz, and Mann, *J.*, 1954, 403.
[3] Mann and Smith, *J.*, 1951, 1898.
[4] Mann and Wilkinson, *J.*, 1957, 3346.
[5] Braunholtz and Mann, *J.*, 1955, 381.

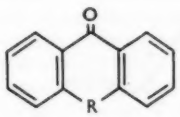
Various unsuccessful attempts to synthesise the arsacridone system, as in (VII), were made by Aeschlimann and McCleland: [6] these usually involved the very difficult cyclisation of an *o*-carboxydiphenylarsine unit (or its acid chloride). Failure was also recorded by Sakellarios.[7]

We find however that 5 : 10-dihydro-10-phenylarsacridine (V) is readily oxidised by hot aqueous potassium permanganate to the 10-phenylarsacridone oxide (VI), which is reduced in turn by sulphur dioxide–hydrochloric acid to the colourless, crystalline arsacridone (VII).

10-Phenylarsacridone (VII) showed the expected chemical inertness. The carbonyl group did not react with hydroxylamine, hydrazine, phenylhydrazine, 2 : 4-dinitrophenylhydrazine, or malononitrile under the normal conditions. It did react, however, with phenylmagnesium bromide to give the alcohol (VIII), a reaction comparable to that shown by analogous acridones. The tertiary arsine group in the arsacridone (VII) also showed marked deactivation, for although the arsacridine (V) was readily quaternised by boiling methyl iodide, the arsacridone (VII) was unaffected in these conditions, and did not apparently react with methyl toluene-*p*-sulphonate below 190—200°. Furthermore, whereas most tertiary arsines react exothermally with cold acetone–hydrogen peroxide, the arsacridone required this boiling reagent for reconversion into the arsine oxide (VI).



(VIII)



(IX)

The arsacridone reacted with ethanolic potassium palladobromide, but the highly insoluble nature of the covalent derivative, $[(C_{19}H_{13}OAs)_2PdBr_2]$, would promote its formation.

If the low reactivity of the carbonyl group and the arsine group is in fact caused by the contribution of the polar form (VIIA), conversion of the 3-covalent arsenic atom into the 4-covalent condition by an external reagent should, by destroying this charge separation, restore the activity of the carbonyl group. Chemical evidence on this point is not readily available, for phenylhydrazine merely reduced the arsacridone oxide (VI) to the arsacridone (VII), and the product of the interaction of phenylhydrazine and the arsacridone methotoluene-*p*-sulphonate could not be crystallised and identified.

The absorption spectra, however, provide strong evidence for the polar separation (VIIA). The infrared carbonyl frequencies of the arsacridone (VII) and related compounds (IX) are shown in the Table. It is noteworthy that the carbonyl frequency of the

Compound	(IX); R =	>CO frequency ($cm.^{-1}$)	Compound	(IX); R =	>CO frequency ($cm.^{-1}$)
10-Phenylanthrone	:CHPh	1662	10-Phenylacridone	:NPh	1632
10 : 10-Diphenylanthrone	:$CHPh_2$	1665	The arsacridone (VII)	:AsPh	1647
Xanthone	:O	1660	The arsacridone oxide (VI)	:As(O)Ph	1662
Thioxanthone	:S	1645			

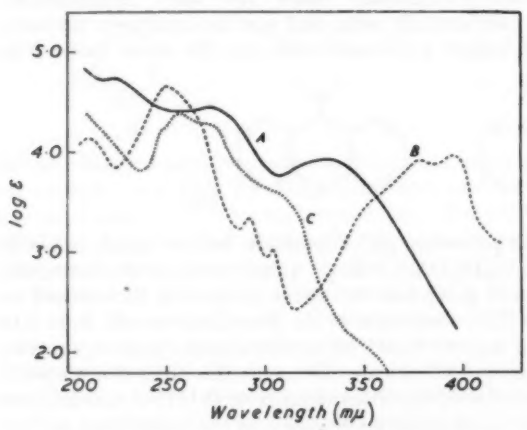
arsacridone (VII) is significantly lower (by *ca.* 15 $cm.^{-1}$) than the normal frequency in comparable anthrones, although the decrease in frequency is less than that shown by 10-phenylacridone, indicating a greater degree of lone-pair–carbonyl interaction in the last compound. Even more decisive is the restoration of the normal frequency in the arsacridone oxide (VI), in which this interaction is impossible. Further, the carbonyl frequency of xanthone is very slightly lower than that of the two anthrones, but the frequency of thioxanthone, in which greater charge separation would be expected, falls to almost that of the arsacridone (VII).

[6] Aeschlimann and McCleland, *J.*, 1924, 2025.
[7] Sakellarios, *Ber.*, 1926, **59**, 2552.

XUM

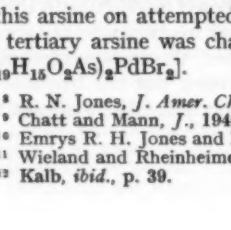
The ultraviolet absorption spectra of 10-phenylacridone and the arsacridone (VII) are not greatly dissimilar (see Fig.), but the region of large absorption which is, by comparison with the spectrum of anthrone,[8] due to the electronic change introduced by the Group V element, has undergone a smaller shift to longer wavelength in the arsacridone than in the acridone, indicating a smaller degree of conjugation in the former compound and accounting for its colourless appearance in contrast to the yellow colour of the acridone.

There is thus considerable chemical and physical evidence that the polar form (VIIA) contributes substantially to the structure of 10-phenylarsacridone (VII), which becomes an addition to the small number of heterocyclic arsenic compounds in which the arsenic atom is apparently linked by a single and a double bond respectively to the two adjacent carbon atoms of the ring. It is noteworthy that these compounds also have the anthracene-type of ring system: there is considerable evidence for the above structure in the 5 : 10-disubstituted arsanthronium ions,[9,10] but at present only weak evidence for its existence in the products claimed to be phenarsazine[11] and arsanthren.[12]

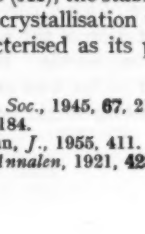


A, 10-*Phenylarsacridone* (VII).
B, 10-*Phenylacridone*.
C, *Anthrone, copied from R. N. Jones.*[8]
All in ethanol.

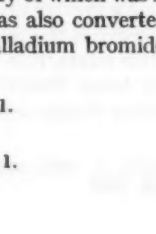
Our earlier attempts to prepare an arsacridone of type (VII) were based on the projected synthesis of *o*-carboxy-*m'*-methoxytriphenylarsine (X; R = OMe), in which it was hoped that the activation of the benzene ring by the methoxyl group would promote subsequent cyclisation. These attempts were discontinued when it was found that *o*-carboxytriphenylarsine (X; R = H) in organic solvents underwent exceptionally rapid



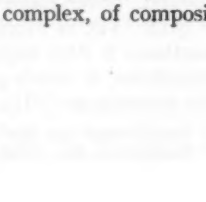
(X)



(XI)



(XIA)



(XII)

conversion into the arsine oxide (XI), the stability of which was so high that the methiodide of this arsine on attempted recrystallisation was also converted into the oxide, although the tertiary arsine was characterised as its palladium bromide complex, of composition $[(C_{19}H_{15}O_2As)_2PdBr_2]$.

[8] R. N. Jones, *J. Amer. Chem. Soc.*, 1945, **67**, 2141.
[9] Chatt and Mann, *J.*, 1940, 1184.
[10] Emrys R. H. Jones and Mann, *J.*, 1955, 411.
[11] Wieland and Rheinheimer, *Annalen*, 1921, **423**, 1.
[12] Kalb, *ibid.*, p. 39.

Evidence that the arsine oxide exists as the zwitterion (XIA) is provided by the infrared spectrum, the salient features of which are closely similar to those shown by 2-carboxyethyldiphenylarsine oxide[13] (XII). The evidence for the structure (XIA) is: (*a*) the spectrum shows bands at 1620 and 1382 cm.$^{-1}$, characteristic of the $\cdot CO_2^-$ ion, but none in the 1680 cm.$^{-1}$ region where a carbonyl group would be manifest; (*b*) there are broad bands at 2900 and 2300 cm.$^{-1}$; (*c*) although there are small sharp bands at 905, 842, and 817 cm.$^{-1}$, there is no dominant absorption in this region comparable to that shown in the spectra of the acids $PhAs(O)[(CH_2)_n \cdot CO_2H]_2$, where $n = 1$ or 3,[13] and attributed to the As:O group. The zwitterion structure (XIA) apparently confers quite exceptional stability, for this compound, unlike normal tertiary arsine oxides, did not form a hydroxy-salt with picric acid or with the stronger inorganic acids.

Experimental

2-Aminodiphenylmethane was prepared by Mann and Stewart's method,[14] and diphenylmethane-2-arsonic acid, 10-arsacridinic acid, and 10-chloro-5 : 10-dihydroarsacridine by the modifications introduced by Hewett *et al.*[15] into Gump and Stoltzenberg's original method.[16]

5 : 10-*Dihydro*-10-*phenylarsacridine* (V).—A solution of 10-chloro-5 : 10-dihydroarsacridine (8·3 g.) in benzene (30 c.c.) was slowly added to a stirred solution of phenylmagnesium bromide prepared from bromobenzene (6·3 c.c., 2 mols.) and magnesium (1·44 g., 2 equivs.) in ether (30 c.c.). When the vigorous reaction had subsided, the mixture was boiled under reflux for 5 min., cooled, and hydrolysed with aqueous ammonium chloride. Removal of the solvents from the dried organic layer left an oil which solidified and on recrystallisation from ethanol afforded the *arsacridine* (V), m. p. 74—75° (9·4 g., 98%) (Found: C, 71·2; H, 4·8. $C_{19}H_{15}As$ requires C, 71·6; H, 4·7%). The methiodide was readily formed in boiling methyl iodide as a gum which when rubbed with acetone formed a solid, m. p. 151—152° (effervescence). This could not be recrystallised, but gave a *methopicrate*, yellow crystals (from ethanol–acetone), m. p. 260° (decomp.) (Found: C, 55·5; H, 3·8; N, 7·7. $C_{26}H_{20}O_7N_3As$ requires C, 55·6; H, 3·6; N, 7·5%).

10-*Phenylarsacridone* (VII).—A stirred suspension of the arsacridine (V) (4·59 g.) in water (100 c.c.) was kept at 70—80° whilst powdered potassium permanganate (4·56 g., 1·00 mol.) was added in *ca.* 0·5 g. portions. The mixture was boiled for 2 min., cooled, and extracted with chloroform (75 c.c.). Removal of the solvent gave the *arsacridine oxide* (VI) (4·90 g., almost 100%), m. p. 238° after crystallisation from acetone (Found: C, 65·6; H, 3·6. $C_{19}H_{13}O_2As$ requires C, 65·6; H, 3·7%). Sulphur dioxide was passed through a suspension of this oxide (4·5 g.) in concentrated hydrochloric acid (50 c.c.) and water (50 c.c.) containing potassium iodide (0·2 g.) for 30 min. The solid deposit, when recrystallised from ethanol, afforded the *arsacridone* (VII) (4·1 g., 95%), m. p. 138—139° (Found: C, 68·5; H, 3·8%; *M*, in boiling acetone, 321, 325. $C_{19}H_{13}OAs$ requires C, 68·7; H, 3·9%; *M*, 332).

A solution of the arsacridone in methyl iodide (with or without the addition of methanol) when boiled for 3 hr. afforded the unchanged arsacridone. A mixture of the arsacridone and methyl toluene-*p*-sulphonate (1·2 mols.), when heated at 120—125° for 2·5 hr., also afforded the arsacridone, but when heated at 200° for 1·5 hr. gave first a dark gum and then, when cold, a glass which, rubbed with acetone, formed a fine solid; recrystallisation of this from acetone afforded the *methotoluene*-p-*sulphonate*, m. p. 200°, in small yield (Found: C, 62·2; H, 4·8. $C_{27}H_{23}O_4SAs$ requires C, 62·5; H, 4·4%).

An acetone solution of the arsacridone, when boiled with dilute hydrogen peroxide for 5 min., and evaporated to dryness, gave the oxide (VI), m. p. and mixed m. p. 238° (from water).

A solution of the arsacridone (VII) (0·70 g.) in benzene (5 c.c.) was added to a Grignard reagent prepared from bromobenzene (0·44 c.c., 2 mols.) and magnesium (0·10 g., 2 equivs.) in ether (5 c.c.). The mixture was boiled for 1 hr., cooled, and hydrolysed as before. The dried organic layer on evaporation gave 5 : 10-*dihydro*-5-*hydroxy*-5 : 10-*diphenylarsacridine* (VIII)

[13] Braunholtz and Mann, *J.*, 1957, 3285.
[14] Mann and Stewart, *J.*, 1954, 4127.
[15] Hewett, Lermit, Openshaw, Todd, Williams, and Woodward, *J.*, 1948, 292.
[16] Gump and Stoltzenberg, *J. Amer. Chem. Soc.*, 1931, **53**, 1428.

XUM

(0·65 g., 75%), m. p. 194° after crystallisation from ethanol (Found: C, 73·1; H, 4·9. $C_{25}H_{19}OAs$ requires C, 73·1; H, 4·7%).

A solution of the arsacridone (0·25 g.) in hot acetone, when treated with potassium palladobromide (0·19 g., 0·50 mol.) in a minimum of water, gave an immediate orange precipitate, which when washed with acetone and water, and recrystallised from dimethylformamide, afforded *dibromodi-*(10-*phenylarsacridone*)*palladium*, m. p. 298° (decomp.) (Found: C, 49·0; H, 3·2. $C_{38}H_{24}O_2Br_2As_2Pd$ requires C, 49·0; H, 2·8%).

The arsacridone oxide (VI) was treated with an excess of phenylhydrazine in ethanol containing acetic acid. The mixture, when boiled under reflux for 2 hr. and poured into water, deposited the arsacridone (VII), m. p. and mixed m. p. 137—138°. The methotoluene-*p*-sulphonate when similarly treated deposited a red gum which was soluble in all the usual solvents and could not be crystallised.

2-*Methyltriphenylarsine.*—A solution of chlorodiphenylarsine (10·0 g.) in ether (50 c.c.) was added to a Grignard reagent prepared from *o*-bromotoluene (9·7 g., 1·5 mols.) and magnesium (1·37 g., 1·5 equivs.) in ether (100 c.c.), which was then boiled for 30 min. The usual working-up gave a solid residue, which on crystallisation from ethanol afforded the *arsine* (9·8 g., 81%), m. p. 63—64° (Found: C, 70·9; H, 5·55. $C_{19}H_{17}As$ requires C, 71·2; H, 5·3%).

A mixture of the arsine (7·0 g.), potassium permanganate (10·2 g., 1·1 equivs.), and water was boiled under reflux for 1 hr., the pink colour disappearing. The mixture, when made alkaline with sodium carbonate, filtered through " Supercel," and acidified with hydrochloric acid, deposited the crude *o-carboxytriphenylarsine oxide* (XI) (4·4 g., 55%), m. p. 237—242°, increased to 246—247° after wasteful recrystallisation from ethanol (Found: C, 62·0; H, 4·2. $C_{19}H_{15}O_3As$ requires C, 62·3; H, 4·1%). The oxide was recovered unchanged after treatment in concentrated ethanolic solution with picric acid, sodium picrate, sodium iodide, or nitric acid.

When sulphur dioxide was passed through a suspension of the oxide (4·2 g.) in concentrated hydrochloric acid (40 c.c.) containing potassium iodide (0·1 g.) for 25 min., an oil separated and slowly became more viscous. A solution of this product in ethanol (7 c.c.), when set aside in a small closed flask at 0° for 4 days, deposited crystals (2·0 g.), m. p. 135—138°, presumably *o*-carboxytriphenylarsine (X; R = H), but a second recrystallisation gave solely the oxide, m. p. and mixed m. p. 245—246°. A solution of the crystals, m. p. 135—138°, in methyl iodide, when boiled for 10 min., deposited a methiodide, m. p. 102—104° (effervescence, rapid heating), but recrystallisation from ethanol again gave the oxide, m. p. and mixed m. p. 245—246°. A solution of the arsine in concentrated sulphuric acid, when heated at 100° for 45 min., cooled, and poured into water, again deposited the oxide.

Aqueous-ethanolic potassium palladobromide was added with shaking to a cold sample of the freshly prepared viscous arsine, which had been washed with aqueous sulphur dioxide and then dissolved in ethanol. *Dibromodi-*(*o-carboxytriphenylarsine*)*palladium* separated as orange crystals, m. p. 255° (decomp.) after washing with water and ethanol and drying at 70°/0·1 mm. (Found: C, 47·1; H, 3·3. $C_{38}H_{30}O_4Br_2As_2Pd$ requires C, 47·2; H, 3·1%). The compound was insoluble in, and unaffected by, boiling methanol, ethanol, acetone, and benzene, but in boiling aqueous ethanol it rapidly decomposed with deposition of palladium.

Bart Reactions.—These reactions formed the basis of a preliminary study of compounds of type (X), and are briefly recorded.

(i) *Dichloro-*m-*methoxyphenylarsine.* *m*-Methoxyphenylarsonic acid,[2] when reduced with sulphur dioxide–hydrochloric acid in the usual way, afforded this *arsine* in 70% yield as a colourless liquid which soon became yellow, b. p. 157°/15 mm. (Found: C, 33·6; H, 3·1. $C_7H_7OCl_2As$ requires C, 33·2; H, 2·8%). An attempted Bart reaction, in which aqueous *o*-tolyldiazonium chloride and a solution of the dichloroarsine in aqueous sodium hydroxide–sodium carbonate were run concurrently into ice-water, yielded *m*-methoxyphenylarsonic acid,[1] m. p. and mixed m. p. 138—141° after crystallisation from water.

(ii) *m*-Nitrobenzenediazonium chloride, when brought into reaction with dichloro-*o*-tolylarsine in alkali, under the conditions used by Blicke and Webster [17] for the preparation of *m*-nitrodiphenylarsinic acid, yielded solely *o*-tolylarsonic acid. The same result was obtained when *m*-nitroaniline was diazotised in 90% ethanol with concentrated sulphuric acid and sodium nitrite, and then treated directly with dichloro-*o*-tolylarsine.

(iii) A solution prepared by adding dichloro-*m*-nitrophenylarsine (5·0 g.), sodium hydroxide (3 g.), anhydrous sodium carbonate (1 g.), and copper sulphate crystals (0·2 g.) to water (100 c.c.)

[17] Blicke and Webster, *J. Amer. Chem. Soc.*, 1937, **59**, 534.

was added during 10 min. to a vigorously stirred solution prepared from *o*-toluidine (2·0 g., 1 mol.), concentrated hydrochloric acid (5 c.c.), and sodium nitrite (1·3 g., 1 mol.) in water (40 c.c.). The mixture was stirred for 30 min., then heated with charcoal and filtered. The filtrate, when made just acid (Congo-red), deposited a pink precipitate; this was purified by dissolution in aqueous sodium hydroxide, which was then boiled with charcoal, filtered, cooled, and again acidified. The fine colourless precipitated powder, which was almost certainly 3 : 3′-*diarsonoazoxybenzene* (2·0 g., 48%), did not melt below 400° (Found: C, 32·55; H, 3·2; N, 6·5. $C_{12}H_{12}O_7N_2As_2$ requires C, 32·3; H, 2·7; N, 6·3%).

This diarsonic acid (2·0 g.) was added during 1 hr. to a boiling, vigorously stirred mixture of iron " pin-dust " (4 g.) and 5% aqueous sodium chloride (20 c.c.). The mixture was boiled under reflux for 3 hr. and, after the addition of sodium hydroxide (0·5 g.), filtered through " Supercel." Evaporation of the filtrate to 30 c.c. and cooling gave orange crystals of 3 : 3′-diarsonoazobenzene (1·2 g., 62%), which after recrystallisation from water did not melt below 400° (Found: C, 33·8; H, 3·1; N, 6·6. Calc. for $C_{12}H_{12}O_6N_2As_2$: C, 33·5; H, 2·8; N, 6·5%). This product is apparently identical with the orange-yellow 3 : 3′-diarsonoazobenzene prepared by Lieb,[18] who states that it effervesces feebly at 240° and then on further heating darkens without melting: he also describes it as extremely difficultly soluble in water.

UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, August 15th*, 1957.]

[18] Lieb, *Ber.*, 1921, **54**, 1511.

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58. *Salt-inclusion Complexes of Zeolites.*

By R. M. BARRER and W. M. MEIER.

Intracrystalline inclusion of salt from aqueous solution and from ionic melts has been investigated for two zeolites with very open anionic frameworks, in one of which, a near-faujasite, the equilibrium uptake of sodium chloride from aqueous solution gives isotherms of the opposite curvature from that of Langmuir's isotherm. The isotherm contour can, however, be interpreted as a Donnan membrane equilibrium, or in terms of the law of mass action.

The silver nitrate inclusion compound formed by a second zeolite, Linde molecular sieve 4*A*, has been demonstrated to have the composition $Ag_{12}[12AlO_2,12SiO_2]AgAlO_2,9AgNO_3$. *X*-Ray study has shown that there is an ordered cluster of nine silver nitrate molecules per large cavity in the structure, and that these are probably arranged with a rock-salt configuration, 5 of the (Ag^+–NO_3^-) pairs in a cluster having one orientation and 4 such pairs being oppositely oriented. In the next cage the 5 and 4 pairs have respectively complementary arrangements to those in the first cluster so that a superstructure is observed, and the dimensions of the tetragonal unit cell thereby produced are $A = 2a$, $C = a$, where a is the cubic unit cell dimension of the parent zeolite. The existence of other complexes in which lithium, sodium, and ammonium nitrates replace silver nitrate has also been demonstrated.

ALUMINOSILICATE crystals in which inorganic salts are distributed throughout the anionic framework are not uncommon in Nature. Typical are the scapolites (marialite, wernerite, and meionite) and some felspathoids (sodalite, nosean, ultramarine, helvite, and cancrinite). In addition to the included salts a sufficient number of cations to ensure electrical neutrality is also dispersed through the framework. In the above crystals the salt is present as anion and cation pairs, but the cation may be indistinguishable from any of the additional cations which neutralise the aluminosilicate framework charge. In such structures as that of sodalite there is one anion–cation pair per cavity in the framework,[1] plus the framework cations. The anions are too large to escape from the cavities but

[1] Jaeger, *Trans. Faraday Soc.*, 1929, **25**, 320.

the cations are mobile, and can be exchanged freely.[2,3] Because of the immobilisation of the anions these ions are incorporated during crystal growth and are not liberated without destruction of the aluminosilicate framework.

Recently still more open-framework aluminosilicates have been synthesised[4,5] in which some of the cavities in the crystals are very large, and have wide "windows" linking them into an interconnected channel system. We now have the possibility of multiple occupancy[6,7] of these large cavities by cation–anion pairs (which we can conveniently call salt "molecules"). Moreover, because of the size of the windows the anions as well as the cations can migrate. The possibility therefore arises of studying reversible distributions of salt molecules between aqueous solutions and the interior of these crystals. Such a study is now presented, together with some structural features of salt-inclusion complexes.

The open aluminosilicate frameworks are stabilised by inclusion of fillers, which may be water molecules or salts. Such open frameworks will indeed only form in the presence of fillers, and quantitative measurements of salt inclusion can therefore indicate conditions which must have arisen in Nature for their formation.

Experimental

Materials.—Two zeolites, which have perhaps the most open aluminosilicate frameworks known, were used. These were Linde molecular sieve 13*X*, or Na-*X*, which is a synthetic near-faujasite,[4,5] and Linde molecular sieve 4*A*, or Na-*A*, which is a synthetic zeolite[4,5] without natural counterpart. The structure of both zeolites is known.[7,8,9] Each can be regarded as an arrangement of three kinds of polyhedral unit, one of which, of intermediate size, is common to each and also to sodalite. The polyhedra are built from $(Si,Al)O_4$ tetrahedra. It is, however, the largest of these polyhedral cages in each crystal which are important here; they open into one another by way of "windows," which are rings of twelve $(Si,Al)O_4$ tetrahedra in the faujasite-type crystals and of eight such tetrahedra in molecular sieve 4*A*. Thus two different interconnected channel systems are produced, one characteristic of each crystal. There is considerable information now available regarding the ion exchange[4,10,11] and the gas-sorbing and molecular-sieve properties of each crystal.[4,6]

"AnalaR" salts such as sodium chloride and silver, lithium, ammonium, and sodium nitrates were employed in the study of inclusion, either in aqueous solution or as their melts. Preliminary experiments revealed that Na-*A* did not occlude detectable amounts of sodium chloride from its concentrated solutions, nor did it undergo salt inclusion during ion exchange, so either this process is very slow, or the salt solutions were insufficiently concentrated. Accordingly salt inclusion by Na-*A* was investigated from ionic melts. With the more open lattice of Na-*X*, however, salt inclusion could be examined from aqueous solutions.

Procedure for Aqueous Solutions.—Weighed samples of Na-*X* were treated in sealed tubes with measured amounts of sodium chloride solution of known concentration. The tubes containing the mixtures were rotated for 4 or 5 days at 25° or 100°. Changes in the concentration of salt at equilibrium were small (~1%) so that the following method of measuring the occluded salt was adopted. The liquid was filtered off in a weighed sintered-glass crucible, and the weight of the wet solid determined. The zeolite was then dried by sucking air through the crucible to constant weight. The difference between the weight of the wet and the dry residue gave the amount of adherent water. Hence the amount, W_1, of adherent sodium chloride was found from the sodium chloride concentration in the filtrate. The crystals were then thoroughly extracted with hot water, and the total amount, W_2, of included and adherent salt

[2] Barrer and Raitt, *J.*, **1954**, 4641.
[3] Barrer and Falconer, *Proc. Roy. Soc.*, 1956, *A*, **236**, 227.
[4] Breck, Eversole, Milton, Reed, and Thomas, *J. Amer. Chem. Soc.*, 1956, **78**, 5963.
[5] Barrer and Bultitude, in preparation.
[6] Barrer and Sutherland, *Proc. Roy. Soc.*, 1956, *A*, **237**, 439.
[7] Barrer, Report to the 10th Solvay Council, Brussels, May 1956, "Physical Chemistry of some Non-stoicheiometric Phases."
[8] Reed and Breck, *J. Amer. Chem. Soc.*, 1956, **78**, 5972.
[9] Bergerhoff, Koyama, and Nowacki, *Experientia*, 1956, **12**, 418.
[10] Barrer, Buser, and Grutter, *Helv. Chim. Acta*, 1956, **39**, 518.
[11] Barrer and Meier, in preparation.

determined. The amount of included salt was then $W_2 - W_1$, the accuracy being about $\pm 10\%$.

Procedure for Ionic Melts.—Inclusion complexes were prepared from Na-*A* and ionic melts in the manner illustrated below for the silver nitrate compound. About 2 g. of Ag-*A* were prepared by ion exchange [11] of Na-*A* by use of silver nitrate solution. The crystals were thoroughly mixed with about 10 g. of finely powdered silver nitrate, and the mixture placed in a small porcelain crucible. The crucible was then heated slowly (to prevent spitting due to over-rapid release of water during isobaric dehydration of the zeolite) to 250—260°, and kept thereat for at least 8 hr., after which the temperature was gradually lowered to room temperature during at least 6 hr. The product was finely ground and then washed quickly twice with cold water to remove the adherent silver nitrate. The inclusion compounds thus obtained were slightly yellow but were photosensitive and became dark grey if exposed to daylight for some time.

Investigation of Composition of Inclusion Complex (Ag-*A*,$AgNO_3$).—As it is almost impossible to prepare inclusion compounds by fusion in which the Ag-*A* lattice is both completely filled with silver nitrate and absolutely free from adherent silver nitrate, since appreciable amounts of the occluded salt (apart from adherent salt) are likely to be removed on continued washing, an e.m.f. method was used to determine the amount of occluded silver nitrate. A weighed quantity of the above unwashed product was finely ground and then added all at once to a vigorously stirred known amount of distilled water. The e.m.f. of the cell

$$\underset{}{Ag} \;|\; \underset{(I)}{AgNO_3} \;\|\; \underset{(II)}{AgNO_3} \;|\; Ag$$

was then determined as a function of time. In the above cell compartment (I) contains the variable silver nitrate content derived from the crystals and compartment (II) is a standard reference concentration. A result is shown in Fig. 1. The silver nitrate concentration rose very steeply in the first few minutes until all the adherent silver nitrate was dissolved. The further increase in the silver concentration clearly obeys the $\sqrt{t}$ diffusion law (t = time) and was regarded as due to extraction of included silver nitrate. This diffusion of intracrystalline silver nitrate from the well-ground powder is assumed to begin at zero time, and the amount of adherent silver nitrate, W_2, could thus be found by graphical extrapolation of the linear part of the graph of Fig. 1. The amount of intracrystalline silver nitrate, W_1, was then $W_1 = W_4 - W_2$, where W_4 is the total quantity of silver nitrate present in the sample, which was determined by standard analytical methods.

The following results were thus obtained for the silver nitrate content of the pure inclusion compound of Ag-*A*: (i) 35·5%, (ii) 34·3%, (iii) 35·1% of $AgNO_3$. The mean value of 35·0% of $AgNO_3$ corresponds to 9·15 molecules of silver nitrate per unit cell of the zeolite, since the samples were anhydrous. This leads to the ideal formula

$$Ag_{12}[12AlO_2,12SiO_2]AgAlO_2,9AgNO_3$$

for the filled zeolite, the term in the square brackets denoting the composition and amount of the anionic framework per unit cell of the original zeolite.

Practically all the included silver nitrate could be extracted within 4 days with hot water in a Soxhlet apparatus, but only 65% of the total silver nitrate content was removed by percolating the sample with water for 10 days at room temperature.

Occlusion Isotherms of Sodium Chloride in Na-*X*.—By the above method we obtained the results in the Table for the amounts of sodium chloride, C_1 (mmoles/g. of anhydrous Na-*X*) in equilibrium with solutions of normality C. When C_1 is plotted against C the

Equilibrium occlusion of sodium chloride by Na-*X*.

Temp.	C of NaCl aq. (N)	C^2	C_1 (millimoles of NaCl/g. of anhydrous Na-*X*)	Temp.	C of NaCl aq. (N)	C^2	C_1 (millimoles of NaCl/g. of anhydrous Na-*X*)
25°	1·90	3·61	0·17	100°	1·00	1·00	0·07
	2·57	6·60	0·31		1·99	3·96	0·24
	3·36	12·32	0·45		3·06	9·38	0·63
	3·40	12·60	0·42		3·98	15·80	0·74
	4·09	16·75	0·74		4·62	21·4	1·21
	4·90	24·0	0·90				

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isotherms have an upward inflexion, and so show a curvature in the opposite sense to that shown by Langmuir's isotherm. The amount of occlusion is thus negligible in dilute solutions, but becomes rapidly more important in very concentrated solutions. It can be seen qualitatively that the chloride ion, even with an accompanying sodium cation, will not be likely freely to enter the negatively charged aluminosilicate framework of the zeolite, unless its concentration in aqueous solution becomes large.

The phenomenon appears to be amenable to treatment from the viewpoint of a Donnan membrane equilibrium. At equilibrium we have the following system:

Solution	*Crystal*
Na^+ C; Cl^- C	Na^+ C_m; R^- C_r; Cl^- C_i

R^- refers to the anionic framework and C_r denotes the concentration of negative charge on the anionic framework which, provided the zeolite does not swell or shrink as a result of occlusion of sodium chloride, is constant. This condition is very nearly fulfilled. Also for electrical neutrality

$$C_m = C_i + C_r \quad . . . . . (1)$$

At equilibrium, any transference of water as a result of salt occlusion being neglected, the Donnan equation takes the form

$$a_i a_m = a_\pm^2 \quad . . . . . (2)$$

We then have from eqns. (1) and (2)

$$C_i(C_i + C_r) = \frac{C_\pm^2 f_\pm^2}{f_i f_m} = \frac{C^2 f_\pm^2}{{}_i f_\pm^2} \quad . . . . . (3)$$

In eqn. (2) a_i and a_m denote the activities of intracrystalline Cl^- and Na^+ and $a_\pm$ is the mean activity of sodium chloride in solution; in eqn. (3), $C_\pm$ is the mean concentration of salt in solution, $f_\pm$ and ${}_i f_\pm$ are the mean activity coefficients of sodium chloride in solution and in the zeolite respectively. ${}_i f_\pm^2 = f_i \cdot f_m$ where f_i and f_m are the activity coefficients of Cl^- and Na^+ within the crystal. If we denote $f_\pm^2/{}_i f_\pm^2$ by R then

$$C_i^2 + C_r C_i - RC^2 = 0 \quad . . . . . (4)$$

The constant concentration C_r is about 12 equiv. per 1000 cm.^{3} of crystals while the Table shows that C_i in terms of moles per 1000 cm.^{3} of crystals is substantially smaller. Thus eqn. (4) approaches

$$C_i = RC^2/C_r \quad . . . . . (5)$$

and provided R does not depend very much upon C or C_i, C_i is proportional to C^2. Thus the observed upward inflexion of the isotherm is explained. Fig. 2 shows C_i plotted against C^2, and demonstrates that eqn. (5), or its more exact counterpart eqn. (4), is satisfactory in form. A little more salt is occluded at 100° (●) than at 25° (○).

If, per mole of sodium chloride included, n moles of water are displaced from crystal to aqueous solution, the inclusion process can be represented as

$$mH_2O_{aq} + m_iH_2O_i + Na^+_{aq} + Cl^-_{aq} \longrightarrow Na^+_i + Cl^-_i + (m+n)H_2O_{aq} + (m_i - n)H_2O_i$$

and the equilibrium constant becomes *

$$(a_i a_m / a_\pm^2)\{(a_{H_2O})_{aq}^n / [(a_{H_2O})_i^n]\} = K \quad . . . . . (6)$$

This reduces to the form of eqn. (4) with $R = K(a_{H_2O})_i^n f_\pm^2 / [(a_{H_2O})_{aq}^n \cdot {}_i f_\pm^2]$ and, again provided R does not depend strongly on C and C_i, leads to the same conclusions.

The foregoing treatment is based on the important assumption that anion-sieve effects do not arise. These effects could inhibit anion uptake entirely in crystals in which cations

* This equilibrium condition can be further simplified by assuming that for the distribution of water between crystals and solution an additional condition is $(a_{H_2O})_i = (a_{H_2O})_{aq}$. This assumption does not change our conclusions.

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FIG. 1.

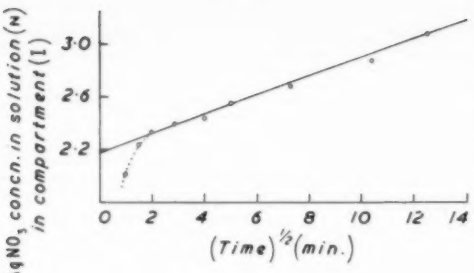


FIG. 2.

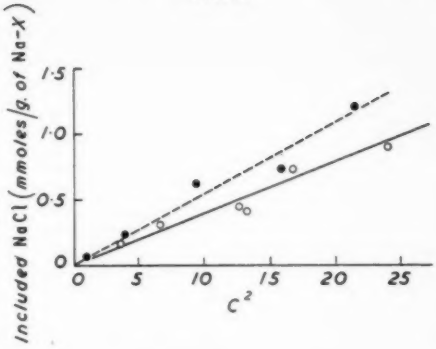


FIG. 3.

FIG. 4.

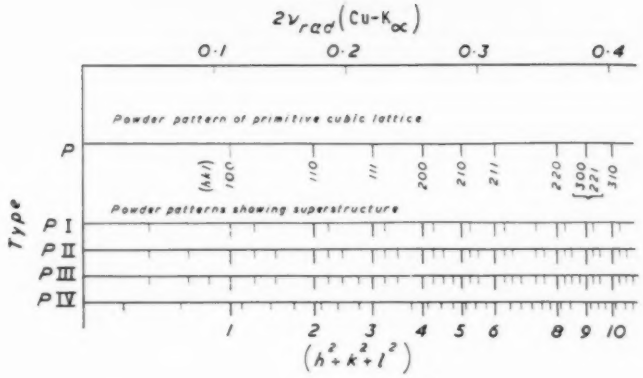


FIG. 5.

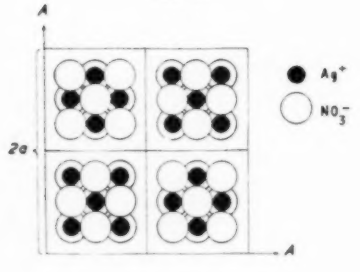


FIG. 6.

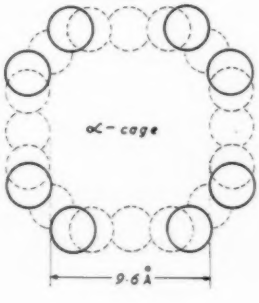
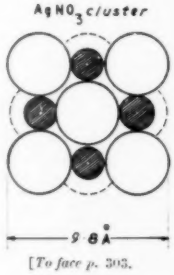


FIG. 7.



[To face p. 303.

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interchange freely, since anions are normally larger than cations. The constancy of the exchanger volume for these crystals contrasts with the processes of swelling and shrinking with gel exchangers. These processes make interpretation of the experimental results for gels more difficult. Thus Bauman and Eichhorn,[12] who studied the uptake of anions by the cation-exchanger Dowex 50, could not interpret their results quantitatively on the basis of a simple Donnan treatment.

X-Ray Investigation of the Inclusion Compound Ag-*A*–$AgNO_3$.—Fig. 3 shows *X*-ray powder photographs of the following substances: (A) Ordinary Ag-*A*; (B) $AgNO_3$ inclusion compound washed twice with cold water; (C) completely extracted inclusion compound; (D) silver nitrate (for comparison). The most striking features in these *X*-ray powder photographs are the additional lines in the powder pattern of the inclusion compound B, which disappear completely on extracting the occluded silver nitrate from the zeolite (C) thus giving the initial pattern, *A*, again. It can easily be seen that these new lines do not correspond to the silver nitrate pattern (D). It must therefore be concluded that they represent superstructure lines, since they cannot be indexed on the basis of the cubic unit cell of Ag-*A* which has a cell constant $a = 12{\cdot}3$ Å. The observed superstructure means that the included phase is ordered with respect to the host lattice and that the particular arrangement of the intracrystalline silver nitrate gives rise to a multiple unit cell. In addition there must be exactly 9 $AgNO_3$ units per unit cell, and hence per large or α-cage in the ordered arrangement, to agree with the composition given earlier (p. 301). Theoretical superstructure patterns were then considered in order to interpret the observed superstructure lines. The simplest of these patterns, which are shown in Fig. 4, are

P I:	$A = 2a$	$B = a$	$C = a$	*P* III:	$A = 2a$	$B = 2a$	$C = 2a$
P II:	$A = 2a$	$B = 2a$	$C = a$	*P* IV:	$A = a$	$B = a$	$C = 3a$

Comparison of the observed pattern with these theoretical patterns revealed that the observed lines were all compatible with pattern *P* II. The lines in the *X*-ray photographs of the filled Ag-zeolite could thus be indexed on the basis of a new tetragonal unit cell with the constants $A = 2a$ and $C = a$, where a is the unit cell constant of Ag-*A*.

Only one arrangement of the 9 silver nitrate units per unit cell could be found which satisfies both the type of superstructure and the available space in the large or α-cages of the structure. This probable arrangement of the Ag^+ and NO_3^- ions is shown in Fig. 5,[13] where the direction of view is along the *C*-axis. The nitrate ions are drawn as spheres and are grouped together with the silver cations in small aggregates or clusters forming a cubic arrangement of the rock-salt type, the unit cell dimensions in two dimensions being thus doubled. It is also interesting that the arrangement leads to an antiparallel polarisation of neighbouring clusters. Figs. 6 and 7 illustrate the available space in the large cage and the size of the suggested silver nitrate clusters respectively. *X*-Ray investigation of this inclusion compound has not been carried further, since the actual positions of the nitrate ions can hardly be located by *X*-rays in the presence of the strongly scattering silver cations. Fig. 3 shows in addition that a slight expansion of the zeolitic framework is brought about by the occlusion of silver nitrate. Measurements revealed a relative expansion of 0·9%.

Quenching of the reactant mixture in the fusion experiment led to products whose rather diffuse *X*-ray patterns (with hardly any superstructure lines) indicated marked disorder. This shows that the gradual cooling of the reactant mixture is essential in the preparation of the filled species. Other inclusion compounds were prepared in the manner as described (p. 301) with molten lithium, sodium, or ammonium nitrates and the respective cationic form of the *A*-zeolite. The melts were held about 20° above the m. p. of the salt used. Extensive salt inclusion was observed in all these cases but quantitative compositions were not obtained because the e.m.f. method could not be applied.

[12] Bauman and Eichhorn, *J. Amer. Chem. Soc.*, 1947, **69**, 2830.
[13] Cf. Barrer and Meier, *Helv. Phys. Acta*, 1956, **29**, 229.

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The powder patterns of all these preparations revealed lattice expansions of about 1% as in the case of the silver nitrate inclusion compound. However, superstructure lines were observed only in the case of the Li-*A*–$LiNO_3$ complex, and this superstructure was of the same type as in the silver nitrate inclusion compound. This means that the arrangement of the included species must be essentially the same in both these cases in spite of the apparent differences in the ionic radii of Ag^+ and Li^+. Moreover, the absence of superstructure lines in the *X*-ray patterns of the sodium nitrate and ammonium nitrate compounds does not necessarily indicate structural differences between these compounds and the silver nitrate adduct. The superstructure may not be observable in these cases since the scattering factors of the Na^+, NH_4^+, and NO_3^- ions do not differ appreciably.

One of us (W. M. M) is indebted to the Schweizerische Nationalfonds for a grant.

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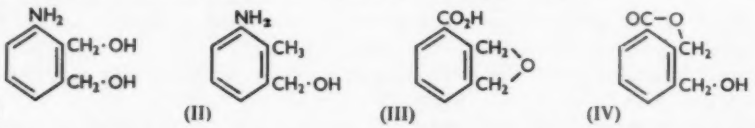
59. *Phthalans. Part I. The Preparation of Phthalan-4-carboxylic Acid.*

By JOHN BLAIR, W. R. LOGAN, and G. T. NEWBOLD.

Phthalan-4-carboxylic acid was prepared from dimethyl 3-aminophthalate.

FOLLOWING earlier studies on the formation of phthalan-4-carboxylic acids, substituted in the benzene ring, by isomerisation of the corresponding 4-hydroxymethylphthalides [1,2] it was desired to synthesise the unknown phthalan-4-carboxylic acid (III). The route envisaged required 3-aminophthalyl alcohol (I) as starting material.



Dimethyl 3-aminophthalate [3] was treated with boiling ethereal lithium aluminium hydride; two products, separated by crystallisation and chromatography, were isolated. The first was the expected 3-aminophthalyl alcohol (I), which was formed in only slightly higher yield at 0°, while the other product, $C_8H_{11}ON$, had m. p. 106—107°. The alcohol (I) was partly converted into the compound $C_8H_{11}ON$ by more vigorous treatment with lithium aluminium hydride. Conover and Tarbell [4] have shown that while reduction by lithium aluminium hydride of benzenoid carbonyl compounds with *o*- or *p*-amino-groups gives the corresponding alcohol under normal conditions, prolonged reaction results in the formation of the corresponding deoxy-compound. The conditions used by these authors were much more drastic than those described in this paper. It therefore appeared that the compound, $C_8H_{11}ON$, must be formulated as 3-amino-2-methylbenzyl alcohol (II), whose preparation as an oil has been described by Erlenmeyer and his collaborators [5] from 2-methyl-3-nitrobenzoic acid by successive conversion into the acyl chloride and the thiobenzyl ester followed by nickel desulphurisation. An unambiguous preparation of the alcohol (II) was therefore desirable; we have accomplished this by catalytically hydrogenating methyl 2-methyl-3-nitrobenzoate and then reducing the resulting amino-ester with lithium aluminium hydride, the compound $C_8H_{11}ON$ (II) then being obtained in good yield. The Swiss workers' product was probably insufficiently purified.

[1] Brown and Newbold, *J.*, 1952, 4878.
[2] Blair and Newbold, *J.*, 1954, 3935; Blair, Logan, and Newbold, *J.*, 1956, 3608; Logan and Newbold, *J.*, 1957, 1946.
[3] Twiss and Heinzelmann, *J. Org. Chem.*, 1950, **15**, 496.
[4] Conover and Tarbell, *J. Amer. Chem. Soc.*, 1950, **72**, 3586.
[5] Sorkin, Krähenbühl, and Erlenmeyer, *Helv. Chim. Acta*, 1948, **31**, 65.

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Replacement of the amino-group of 3-aminophthalyl alcohol (I) by the cyano-group followed by alkaline hydrolysis gave in small yield an acid product, $C_9H_8O_3$, which we regard as phthalan-4-carboxylic acid (III). This acid has presumably been formed by the base-catalysed isomerisation of 4-hydroxymethylphthalide (IV), formed initially. We did not obtain the phthalide (IV) from the uncrystallisable neutral fraction of the hydrolysis. Brown and Newbold [1] have shown that 5 : 6-dimethoxyphthalan-4-carboxylic acid is converted into 4-hydroxymethylmeconin (4-hydroxymethyl-6 : 7-dimethoxyphthalide) when heated with acid. This method being used phthalan-4-carboxylic acid gave a neutral solid, not obtained pure, but whose infrared spectrum in Nujol showed hydroxyl (3390 cm.$^{-1}$) and phthalide-carbonyl (1770 cm.$^{-1}$) peaks, indicating that the product was crude 4-hydroxymethylphthalide (IV).

Experimental

Ultraviolet-light absorptions were determined in ethanol.

Methyl 2-Methyl-3-nitrobenzoate.—An ice-cooled solution of 2-methyl-3-nitrobenzoic acid [5] (2·55 g.) in methanol (30 c.c.) was treated with excess of an ethereal solution of diazomethane, and the reaction solution kept overnight. Methyl 2-methyl-3-nitrobenzoate (2·2 g.) formed felted needles, m. p. 65—66° (from aqueous methanol) (Found: C, 55·3; H, 4·6. Calc. for $C_9H_9O_4N$: C, 55·4; H, 4·65%). The m. p. of the ester obtained [6] from the acid chloride is 66°.

3-Aminophthalyl Alcohol.—Dimethyl 3-aminophthalate (2·56 g.), prepared from dimethyl 3-nitrophthalate (3·12 g.) by catalytic reduction in ethyl acetate with Raney nickel catalyst [7] (1·2 g.; W-2), was dissolved in ether (100 c.c.) and added dropwise during 15 min. to a stirred refluxing solution of lithium aluminium hydride (2 g.) in ether (200 c.c.). After 2½ hr. at the boiling point the mixture was cooled to 0° and excess of hydride decomposed by addition of crushed ice. The ethereal layer was separated and the aqueous phase extracted with ether (100 c.c.). The combined ethereal solution was washed with water, dried (Na_2SO_4), and evaporated. Crystallisation of the residue (0·90 g.) from benzene–ethyl acetate–light petroleum (b. p. 60—80°) gave material (0·36 g.; mother liquor *A*) which after several crystallisations from benzene gave *3-aminophthalyl alcohol* (0·25 g.; 14%) as needles, m. p. 96—97° (Found: C, 63·0; H, 6·7. $C_9H_{11}O_2N$ requires C, 62·7; H, 7·2%); $\lambda_{max.}$ 2080 (ε = 29,000), 2410 (ε = 6000), and 2960 Å (ε = 2300). Acetic anhydride–pyridine treatment on the steam-bath for 3 hr. gave the *triacetate* as needles, m. p. 122—122·5° [from benzene–ether–light petroleum (b. p. 60—80°)] (Found: C, 60·5; H, 5·8. $C_{14}H_{17}O_5N$ requires C, 60·2; H, 6·1%); $\lambda_{max.}$ 2075 (ε = 29,800) and 2340 (ε = 6300), $\lambda_{infl.}$ 2700 Å (ε = 1000).

When this reduction was carried out at 0° during 40 hr. the yield of pure 3-aminophthalyl alcohol was 16%.

3-Amino-2-methylbenzyl Alcohol.—(*a*) Mother liquor *A* (see above) was concentrated to half-bulk, and light petroleum (b. p. 60—80°) added. The crystals (0·41 g.) which separated on cooling were chromatographed in benzene (30 c.c.) on alumina (12 g.). Elution with benzene (100 c.c.) and ether (100 c.c.) followed by evaporation of the combined eluates and crystallisation of the residue from benzene gave *3-amino-2-methylbenzyl alcohol* as needles, m. p. 106—107° (Found: C, 70·1; H, 7·8; N, 10·3. $C_9H_{11}ON$ requires C, 70·0; H, 8·1; N, 10·2%); $\lambda_{max.}$ 2070 (ε = 26,800), 2355 (ε = 6300), and 2900 Å (ε = 2000). The *diacetate*, prepared as described for the triacetate above, formed felted needles, m. p. 147·5—148° [from benzene–light petroleum (b. p. 60—80°)] (Found: C, 65·6; H, 6·4; N, 6·7. $C_{13}H_{15}O_3N$ requires C, 65·1; H, 6·8; N, 6·3%); $\lambda_{max.}$ 2110 (ε = 21,500), $\lambda_{infl.}$ 2310 Å (ε = 6400). Further elution of the column with ether–methanol and methanol gave 3-aminophthalyl alcohol, m. p. 96—97° (108 mg.).

(*b*) Methyl 3-amino-2-methylbenzoate (1·53 g.), prepared by catalytic hydrogenation of the corresponding nitro-compound over Raney nickel at room temperature and atmospheric pressure, was added in ether (50 c.c.) during 20 min. to a stirred, refluxing suspension of lithium aluminium hydride (0·8 g.) in ether (100 c.c.). After 2½ hours' refluxing the product was isolated *via* ether. Evaporation gave a solid (1·28 g.) which after crystallisation and sublimation at 75°/10^{-3} mm. had m. p. 106—106·5° alone or on mixing with preparation (*a*). The infrared spectra of preparations (*a*) and (*b*) in Nujol mull were identical.

[6] van Scherpenzeel, *Rec. Trav. chim.*, 1901, **20**, 149.
[7] Cf. ref. 3.

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(*c*) A solution of 3-aminophthalyl alcohol (0·4 g.) in tetrahydrofuran (30 c.c.) was added to a stirred, refluxing suspension of lithium aluminium hydride (0·3 g.) in ether (75 c.c.). After 2½ hr. the product was isolated and purified by chromatography as in (*a*). 3-Amino-2-methylbenzyl alcohol (246 mg.) formed felted needles (from benzene), m. p. 106—107·5° undepressed on mixing with preparation (*a*). Elution of the column with chloroform–methanol (19 : 1) gave unchanged 3-aminophthalyl alcohol (140 mg.), m. p. and mixed m. p. 93—97·5°.

Phthalan-3-carboxylic Acid.—3-Aminophthalyl alcohol (1·0 g.) in hydrochloric acid (1·86 c.c.; *d* 1·16) and water (18 c.c.) was diazotised. Meanwhile a solution of anhydrous nickel chloride (1·32 g.) and potassium cyanide (1·62 g.) in water (10 c.c.) was boiled for 2 min., cooled, and neutralised with sodium carbonate (0·36 g.). To this solution, at <5°, was added the diazonium solution which had been neutralised with sodium carbonate. After being kept at room temperature overnight the mixture was filtered (residue *B*) and the filtrate extracted with ether (3 × 50 c.c.). The combined ethereal extracts were washed with water, dried (Na_2SO_4), and evaporated to a brown gum (222 mg.). Residue *B* was extracted with chloroform (2 × 50 c.c.) to yield a gum (246 mg.). The combined gums were heated under reflux with aqueous potassium hydroxide (25 c.c.; 10%) for 3 hr. The cooled solution was acidified (Congo red) with hydrochloric acid (*d* 1·16), and the precipitate extracted with chloroform (3 × 25 c.c.). The combined extracts were washed with aqueous sodium hydrogen carbonate (2 × 50 c.c.; 10%) and water and dried (Na_2SO_4). Evaporation gave an intractable red gum (72 mg.). The alkaline washings were acidified (Congo-red) with hydrochloric acid (*d* 1·16) and extracted with chloroform. The dried (Na_2SO_4) extract on evaporation gave a solid (114 mg.) which on crystallisation from benzene (charcoal) gave *phthalan-4-carboxylic acid* as needles, m. p. 195·5—199° (Found: C, 65·5; H, 5·2. $C_9H_8O_3$ requires C, 65·85; H, 4·9%); $\lambda_{max.}$ 2065 (ε = 19,600), 2300 (ε = 9500), and 2850 Å (ε = 2200).

Attempted Preparation of 4-Hydroxymethylphthalide.—Phthalan-4-carboxylic acid (32 mg.) was heated under reflux for 3 hr. with hydrochloric acid (10 c.c.; 5N). The cooled solution was diluted with water (30 c.c.) and extracted with chloroform (3 × 40 c.c.); the combined extracts were washed with aqueous sodium hydrogen carbonate (2 × 25 c.c.) and water and dried (Na_2SO_4). Evaporation of the solvent, sublimation of the residue at 70°/10^{-3} mm. and trituration of the sublimate with a little dry ether gave a white solid, m. p. 103—105·5° (2 mg.).

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[*Received, September 10th*, 1957.]

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60. *The Reduction of Diphosphopyridine Nucleotide and Some Model Compounds by X-Rays.*

By GABRIEL STEIN and A. J. SWALLOW.

Aqueous solutions containing diphosphopyridine nucleotide and ethanol, in the absence of oxygen, when irradiated with *X*-rays, produce acetaldehyde, hydrogen, and a reduced form of the nucleotide.[1,2] Adenosine 5′-phosphate is not a good model for diphosphopyridine nucleotide in this reaction, but 1-alkylnicotinamide chlorides give reduction products. In the case of diphosphopyridine nucleotide, the value of the reduction yield, together with the number of reducing equivalents of the product, strongly suggests that the product is a dimer. The reaction mechanism is discussed and free-radical equations are put forward.

DIPHOSPHOPYRIDINE NUCLEOTIDE can be reduced by irradiating its solutions in oxygen-free water containing excess of ethanol, with *X*- or γ-rays.[1,2] The reaction proceeds through the agency of free hydroxyethyl radicals, and the product differs from the normal enzymic reduction product. The reaction is of interest in connection with the mechanism of dehydrogenase action,[1,2] because of its implications for radiobiology,[3] and because of

[1] Swallow, *Biochem. J.*, 1953, **54**, 253.
[2] *Idem, ibid.*, 1955, **61**, 197.
[3] *Idem*, in "Progress in Radiobiology," ed. by Mitchell, Holmes, and Smith, Oliver and Boyd, Edinburgh, 1956, p. 317.

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the novel nature of the method of reduction and of the product. This method of reduction and ordinary chemical methods have already been compared,[4] but we have investigated it further in order to ascertain the nature of the reduced product and the reaction mechanism. Some of this work has been briefly reported elsewhere.[3, 5]

FIG. 1. *Absorption curves of* 1-*methylnicotinamide chloride solution after irradiation with* 78,000 r; ●, *control*; +, *presence of air*; ○, *absence of oxygen.*

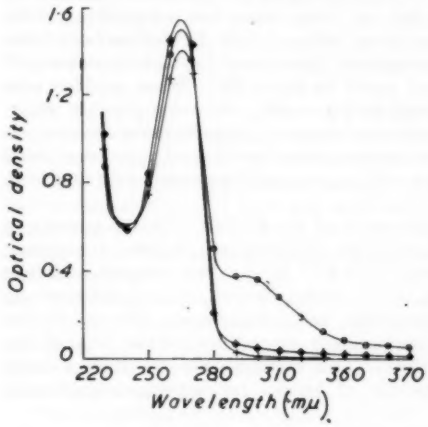
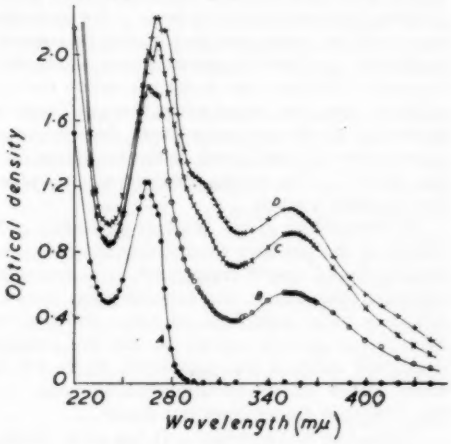


FIG. 2. *Absorption curves of oxygen-free* 1-*methylnicotinamide chloride solutions irradiated in the presence of* 0·5M-*ethanol*; *A, control diluted* 4 ⟶ 3; *B,* 39,000 r; *C,* 78,000 r; *D,* 156,000 r.



EXPERIMENTAL

Irradiation Arrangements.—Two Victor Maximar *X*-ray sets were used, one operated at 220 kvp, with the radiation filtered through 1 mm. of aluminium, and the other at 190 kvp, the radiation being unfiltered. Dosimetry was by the ferrous sulphate method,[6] the yield being taken as $G = 15{\cdot}5$ molecules of ferrous ion oxidised per 100 ev absorbed. The temperature of irradiation was normally 20—30° but during the large-scale reduction of 1-methylnicotinamide chloride the temperature rose to about 40°.

Spectrophotometric Measurements.—1 cm. quartz spectrophotometer cuvettes were used. The absorption curves shown in Figs. 1 and 2 were on undiluted solutions, except where stated otherwise.

Materials.—Diphosphopyridine nucleotide (from the Sigma Chemical Company, U.S.A., and from C. F. Boehringer and Soehne, Germany), crystalline yeast alcohol dehydrogenase (from C. F. Boehringer and Soehne), and adenosine 5′-phosphate (from Schwarz Laboratories, U.S.A.) were used as received. Methylene-blue was a commercial product, recrystallised three times from water. 1-Methyl- and 1-propyl-nicotinamide and chloride were prepared from nicotinamide by the method of Karrer *et al.*[7] Water was distilled from alkaline permanganate. Other chemicals were of " AnalaR " purity.

Spectrophotometric Measurements without Exposure to Oxygen.—The ultraviolet absorption curves given previously [1, 2] were obtained after tipping of irradiated solutions into spectrophotometer cuvettes for measurement. As it seemed possible that exposure to air at this stage could affect the results, the experiments have been repeated in an enclosed system. Air-free aqueous solutions of diphosphopyridine nucleotide (3×10^{-4}M) were irradiated with a dose of 39,000 r. The results obtained were as before, *i.e.*, a product absorbing at 340 mμ was formed

[4] Stein, *J. Chim. phys.*, 1955, **52**, 634; Stein and Stiassny, *Nature*, 1955, **176**, 734; Ke, *Arch. Biochem. Biophys.*, 1956, **60**, 505.
[5] Stein and Swallow, *Nature*, 1954, **173**, 937.
[6] Donaldson and Miller, *J. Chim. phys.*, 1955, **52**, 578; Haybittle, Saunders, and Swallow, *J. Chem. Phys.*, 1956, **25**, 1213.
[7] Karrer, Schwarzenbach, Benz, and Solmssen, *Helv. Chim. Acta*, 1936, **19**, 811.

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when solutions were 0·5M in ethanol, but there was no product in absence of ethanol. Measurement for Tables 1 and 2 were made without exposure to air.

Enzymic Determination of Yield.—*ca.* 3×10^{-4}M-Diphosphopyridine nucleotide solutions, 0·5M in ethanol and at pH 7·8, were irradiated with an *X*-ray dose of 20,000 r. The irradiated solutions were diluted and sodium hydroxide added. The optical density at 340 mμ was measured, alcohol dehydrogenase was added to convert unchanged diphosphopyridine nucleotide into the dihydro-form, and the optical density was again measured. Final pH's were about 9. The difference between the first and the second optical density reading is a measure of unchanged diphosphopyridine nucleotide, and the initial concentration was calculated from control experiments with unirradiated solutions. The yield of diphosphopyridine nucleotide altered by radiation was calculated to be $G = 6{\cdot}9$ molecules/100 ev. This value was independent of the source of the nucleotide and should be correct to about 10%. If all the diphosphopyridine nucleotide had been converted into a dihydro-compound, then from the optical density of irradiated solutions the molar extinction coefficient would be $3{\cdot}2 \times 10^3$. If the product were a dimer, then the molar extinction coefficient would be $6{\cdot}4 \times 10^3$. To avoid possible uncertainty due to the enzyme method, these experiments were repeated, using however the spectrophotometric method based on the formation of a cyanide complex by the unchanged nucleotide ion (DPN^+). The results obtained gave a value for $-G_{DPN^+}$ in good agreement with that from the enzymic method.

Determination of the Number of Reducing Equivalents of the Product.—In irradiations as above, if the product were a dihydro-compound with two reducing equivalents, the optical density found would correspond to a concentration of $2{\cdot}4 \times 10^{-4}$N. For a dimer with two reducing equivalents, the concentration would be $1{\cdot}2 \times 10^{-4}$N. 0·6 ml. of this solution was mixed *in vacuo* with 3 ml. of $4{\cdot}6 \times 10^{-5}$N-methylene-blue, and reduction was followed by the decrease in optical density at 655 mμ. From the amount of methylene-blue reduced the irradiated solution was calculated to be $1{\cdot}1 \times 10^{-4}$N. This method gave the correct result when tested on dihydrodiphosphopyridine nucleotide of known concentration, confirming the view that the product is a dimer.

Adenosine 5′-Phosphate.—It has been shown elsewhere [2] that the product from diphosphopyridine nucleotide, which absorbs at 340 mμ, is a reduced form. Reduction at the nicotinamide end of the molecule seems probable, but to eliminate the possibility that the adenine end is concerned we irradiated $2{\cdot}8 \times 10^{-4}$M-solutions of adenosine 5′-phosphate in 0·01M-pyrophosphate–hydrochloric acid buffer at pH 7·8 with an *X*-ray dose of 78,000 r. The optical density of the solution at 260 mμ was decreased by irradiation whether dissolved oxygen was present or not. Ethanol (0·5M) prevented the decrease in the presence of air, but in the absence of air there was a large decrease in optical density at 260 mμ and an increase below 235 mμ and at 290—300 mμ. However, in no case was there an increase near 340 mμ of the type found for diphosphopyridine nucleotide. It is concluded that the appearance of the absorption band at 340 mμ cannot be ascribed to a change at the adenine moiety, although it is possible that the small decrease at 260 mμ which is also observed [2] may be partly due to a change at this part of the molecule.

1-*Alkylnicotinamide Chlorides.*—Methylnicotinamide chloride was chosen as a model for the nicotinamide end of diphosphopyridine nucleotide. The absorption curve of $3{\cdot}9 \times 10^{-4}$M-solutions, irradiated with 78,000 r in the presence of air at pH 7·8, is little affected (Fig. 1), but in absence of oxygen (Fig. 2) there is an increase in absorption at 290—300 mμ which is found also when the solution is saturated with hydrogen. Fig. 2 shows also that irradiation of oxygen-free solutions 0·5M in ethanol increases absorption at 355 mμ, this resembling the increase at 340 mμ obtained with diphosphopyridine nucleotide under these conditions. In the present case, the optical density increases near 275 mμ, behaviour not observed with diphosphopyridine nucleotide. However, many of the properties of our irradiated chloride resemble those of irradiated diphosphopyridine nucleotide. In particular, when 0·1 ml. of N-hydrochloric acid was added to 3 ml. of an irradiated solution, the absorption bands at 355 and 275 mμ disappeared and a new band appeared at 295 mμ: this change occurred slowly even on storage without addition of acid, but was less pronounced at pH 10·4 than at pH 7·8. Irradiated solutions did not fluoresce under Wood's light (pH 7·8 or 10·4) but a pale blue fluorescence appeared on addition of 1 : 4-dihydro-1-methylnicotinamide, prepared from 1-methylnicotinamide chloride and sodium dithionite. Irradiated solutions were bright yellow; solutions of 1 : 4-dihydro-1-methylnicotinamide with the same optical density at 360 mμ were paler.

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Isolation of the Reduction Product of 1-*Methylnicotinamide Chloride.*—A 0·034% aqueous solution of the methochloride containing 3% of ethanol was prepared in a carbonate–bicarbonate buffer at pH 10·2. 250 ml. of the solution in a round-bottomed flask were deaerated by evacuation, filling with oxygen-free nitrogen (British Oxygen Company), and two repetitions of this cycle. The solution was given a dose of 260,000 r (5·5 hr.), becoming bright yellow. The aqueous solution was evaporated to about 10 ml. under reduced pressure of nitrogen. 1 ml. of N-sodium hydroxide was added, and the solution extracted six times under nitrogen with butan-1-ol (previously washed with N-sodium hydroxide). The butanol extract was dried (Na_2SO_4) and evaporated under reduced pressure of nitrogen to leave an orange oil. This was left overnight in a vacuum-desiccator, then extracted, under nitrogen, with chloroform. The chloroform extract was evaporated under nitrogen, and a solid which separated was filtered off. The residual oil was dissolved in a minimum of methanol and evaporated to dryness. This was repeated and the oil finally dried at room temperature *in vacuo*. The final product was a golden-brown sticky solid.

It seems from the experiments described that 1-methylnicotinamide chloride in many ways resembles diphosphopyridine nucleotide whereas adenosine 5′-phosphate does not. The irradiation product of the methochloride was too labile to be recrystallised. It did not fluoresce under Wood's light whereas 1 : 4-dihydro-1-methylnicotinamide exhibited a brown fluorescence in the solid state and was less soluble in chloroform. An aqueous solution of the irradiation product (1 mg./ml.) had pH ~6. It reduced silver nitrate and did not contain chloride. It decolorised methylene-blue solutions at the same rate as 1 : 4-dihydro-1-methylnicotinamide. A solution at pH 11 exhibited absorption maxima at 278 and 355 mμ.[5] Wallenfels and Schüly [6] also obtained a reduced nicotinamide derivative possessing two absorption bands. The solution showed only a slight pale green fluorescence which was very much less than that of 1 : 4-dihydro-1-methylnicotinamide. On addition of acid, the absorption maxima shifted irreversibly to give a single peak at 295 mμ, like that given by 1 : 4-dihydro-1-methylnicotinamide.

The properties of the irradiation product show it to be a reduced form of the methochloride different from 1 : 4-dihydro-1-methylnicotinamide. Reduction at the amide group cannot explain the properties; the product might be a dihydro-compound (I) or (II) [7] or a dimer, *e.g.*, (III; R = Me).[8]

As the methochloride did not crystallise, we examined the propylochloride. This behaves on irradiation in a similar manner to the methochloride, except that it gives a crystalline product,[4] whose properties differ from those of the dithionite reduction product; the elementary analysis is consistent with a dihydro-structure and the previous titrations [4] support this. The structure of the product is therefore probably (I or II; R = Pr^n). Further work on this compound is in progress.

On irradiation of solutions of the propylochloride at various concentrations in the presence of various amounts of ethanol at pH 9·2 the optical density at 360 mμ rose linearly with dose up to 37,500 r in every case except for $3·9 \times 10^{-5}$M-solutions which were 0·5M in ethanol (for which the optical density reached a maximum at 10,000 r) and $3·9 \times 10^{-4}$M-propylochloride solutions 10^{-2}M or 2×10^{-2}M in ethanol (for which a slight downward curve was noted). As a measure of relative yield under the various conditions, the small optical density of a control solution was subtracted from the optical density resulting after 10,000 r. Results given in Tables 1 and 2 show that the yield is little affected by the concentration of the reactants, and therefore here there is no chain reaction.

TABLE 1. *Effect of concentration of* 1-*propylnicotinamide chloride on yield of substance absorbing at* 360 mμ. (0·5M-EtOH.)

Propylochloride concn. (M)	$3·9 \times 10^{-1}$	$3·9 \times 10^{-2}$	$3·9 \times 10^{-3}$	$3·9 \times 10^{-4}$	$3·9 \times 10^{-5}$
Optical density at 360 after 10,000 r *minus* initial optical density	0·22	0·27	0·275	0·23	>0·15

TABLE 2. *Effect of concentration of ethanol on yield of substance absorbing at* 360 mμ. ($3·9 \times 10^{-4}$M-1-*propylnicotinamide chloride.*)

EtOH concn. (M)	3·0	1·0	0·5	0·1	0·05	0·02	0·01
Optical density (as Table 1)	0·24	0·235	0·225	0·21	0·20	0·19	0·17

[5] Wallenfels and Schüly, *Angew. Chem.*, 1955, **67**, 517.
[6] Tompkins and Schmidt, *Univ. Calif. Pub. Physiol.*, 1943, **8**, 247.

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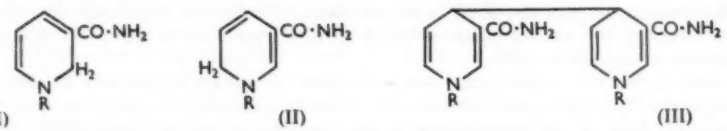
Discussion

Nature of the Reduction Product of Diphosphopyridine Nucleotide.—As Karrer and his collaborators recently emphasised,[10] the reduction of *N*-substituted nicotinamide derivatives is highly complex, and in particular is strongly dependent on the nature of the substituent. The reduction of diphosphopyridine nucleotide itself does not, therefore, necessarily give rise to the same type of product as is obtained from the model compounds. Information bearing on the nature of the product as been obtained from a determination of the yield of diphosphopyridine nucleotide reduced by irradiation in aqueous solution containing ethanol. Approximate values have been estimated previously from the optical density of irradiated solutions at 340 mμ on the assumption that the product has the same extinction coefficient as dihydrodi-



phosphopyridine nucleotide.[11] This method can only give a very rough estimate because the product is *not* dihydrodiphosphopyridine nucleotide. Moreover, previous spectrophotometric results have been only semi-quantitative. The yield has now been measured enzymically and found to be $G = 6{\cdot}9 \pm 0{\cdot}6$ molecules of diphosphopyridine nucleotide reduced per 100 ev absorbed. In view of the general agreement that the yield of radicals in irradiated water is about $G = 6$ radicals per 100 ev absorbed [12] it is difficult to explain a reduction yield as high as G 6·9 without postulating either that the reduction is a one-equivalent one, in which case the product cannot be a dihydro-compound, or that the reaction involves a chain mechanism. However, the reaction does not show the features of a chain reaction, and, in particular, the yield of acetaldehyde on irradiation of ethanolic $2{\cdot}7 \times 10^{-3}$M-diphosphopyridine nucleotide is the same as that from $2{\cdot}7 \times 10^{-4}$M-solutions.[1] To explain the high yield we therefore conclude that the reduction is a one-equivalent one, so that the product does not possess structure (I) or (II; R = ribose-pyrophosphate-ribose-adenine). Additional weight is lent to this argument from related work with methylene-blue,[13] *p*-benzoquinone,[14] and riboflavin.[15] In the case of methylene-blue, where reduction involves two equivalents, the yield has recently been found to be G 3·1. From benzoquinone (irradiated in the presence of excess of formic acid) the yield of quinol was 2·7—2·8, except at high quinone : formic acid ratios where different effects (which could not explain the diphosphopyridine nucleotide results) were evident. For riboflavin, where only one reducing equivalent is needed to produce the stable semiquinone free radical of riboflavin, the yield has been found to be G 6·6.

The value of the yield of diphosphopyridine nucleotide reduced strongly supports the idea that the reduction product is a dimer such as (III), and this is confirmed by measurements of the number of reducing equivalents of the product, measured against methylene-blue. It is therefore highly probable that the product is a dimer, though not necessarily (III), and the two halves of the molecule may be joined elsewhere than at position 4 in the pyridine rings.

Mechanism of the Reduction of Diphosphopyridine Nucleotide.—The principal facts to be accounted for are: (1) the yield of dimer formed by irradiation is G 3·4 molecules/100 ev (*i.e.*, half the yield of diphosphopyridine nucleotide reduced); (2) the acetaldehyde yield [1] in the system is G 5·9 molecules formed/100 ev; (3) the hydrogen yield is G 3·2 molecules formed/100 ev.[2]

We consider the available evidence to exclude participation of sub-excitation electrons [16] in the reaction. The starting point of this discussion must then be the reaction: [17]

$$H_2O \longrightarrow\!\!\!\!\sim\!\!\!\!\rightarrow H + OH \qquad \ldots\ldots\ldots \quad (I)$$

[10] Brook, Blumer, Krishna, Schnell, and Karrer, *Helv. Chim. Acta*, 1956, **39**, 667.
[11] Barron, Johnson, and Cobure, *Radiation Res.*, 1954, **1**, 410.
[12] Hart, *Ann. Rev. Phys. Chem.*, 1954, **5**, 139.
[13] Day and Stein, unpublished work.
[14] Baxendale and Smithies, *Z. phys. Chem.* (*Frankfurt*), 1956, **7**, 242.
[15] Swallow, *Nature*, 1955, **176**, 793.
[16] Weiss, *J. Chim. phys.*, 1955, **52**, 539; Platzman, *Radiation Res.*, 1955, **2**, 1.
[17] Weiss, *Nature*, 1944, **153**, 748.

This reaction is essentially true for "ideal" *X*-rays,[18] but with ordinary *X*- and γ-rays it is usually necessary to allow for reactions such as the formation of molecular hydrogen and hydrogen peroxide.[19] However, the accuracy of the experiments discussed here does not merit a detailed discussion of minor reactions and we therefore feel justified at first in discussing only the principal reaction, *i.e.*, reaction (1).

When aqueous ethanol is irradiated in the absence of oxygen, the products include acetaldehyde, hydrogen, and butane-2 : 3-diol.[20] The yield of hydrogen is high (G = 2·8 molecules/100 ev) [2] and is probably due to the reaction:

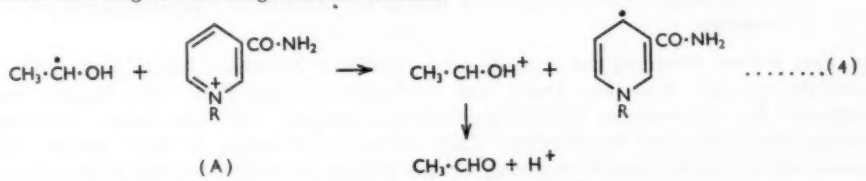
$$H + CH_3{\cdot}CH_2{\cdot}OH \longrightarrow H_2 + CH_3{\cdot}\dot{C}H{\cdot}OH \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

There is growing evidence that this type of reaction occurs, and in particular a similar reaction has recently been put forward for methanol.[21] The view that the free radicals resulting from the oxidation of alcohols are hydroxyalkyl rather than alkoxyl is supported by the detection of glycols in irradiated solutions.[20, 21]

The hydroxyl radicals produced in reaction (1) react with ethanol according to the well-established reaction:

$$OH + CH_3{\cdot}CH_2{\cdot}OH \longrightarrow H_2O + CH_3{\cdot}\dot{C}H{\cdot}OH \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

The experiments with diphosphopyridine nucleotide were conducted with ethanol concentrations of 5×10^{-1}M and diphosphopyridine nucleotide concentrations of 3×10^{-4}M, so that ethanol would be likely to protect the nucleotide from the free radicals formed in reaction (1). It seems that no part of diphosphopyridine nucleotide is sufficiently "radiosensitive," compared with ethanol, for this expectation to be improbable,[22] and further the results with air-saturated solutions confirm the protection afforded by ethanol to diphosphopyridine nucleotide. The reduction of tetrazolium salts by Fenton's reagent in the presence of ethanol [23] has confirmed the reducing action of hydroxyethyl radicals and it is therefore highly probable that diphosphopyridine nucleotide is being reduced by such radicals, probably to give a resonance-stabilised free radical according to the charge-transfer reaction:



The diphosphopyridine nucleotide radicals so formed then dimerise to give the final reduction product represented tentatively as (III).

From these equations, starting with a yield of G = 3 for reaction (1), we can calculate the yield of the various products. The molecular yield of hydrogen (G_{H_2} 0·5), which has so far been neglected, must now be added to the yield of hydrogen calculated from reaction (2). The total reaction is then given by reaction (5).

$$H + OH + 2C_2H_5{\cdot}OH + 2\,(A) \longrightarrow 2CH_3{\cdot}CHO + 2H^+ + H_2 + H_2O + (III) \quad (5)$$

$-G_{calc} = 6$	$G_{calc} = 6$	$G_{calc} = 3 + 0{\cdot}5 = 3{\cdot}5$	$G_{calc} = 3$
$-G_{found} = 6{\cdot}9$	$G_{found} = 5{\cdot}9$	$G_{found} = 3{\cdot}2$	$G_{found} = 3{\cdot}4$

It will be seen that the experimental value for $-G_{DPN}$ is greater than $+G_{CH_3{\cdot}CHO}$, whilst the values calculated for reaction (5) are equal. On the other hand, less hydrogen is evolved than the calculated G_{H_2}. This may be due to some of the hydrogen atoms' being used up in reducing the ion DPN^+.

[18] Stein and Swallow, in "Advances in Radiobiology," Oliver and Boyd, Edinburgh, 1957, p. 16.
[19] Allen, *Radiation Res.*, 1954, **1**, 85.
[20] Scholes, *J. Chim. phys.*, 1955, **52**, 640.
[21] McDonell, *ibid.*, p. 208.
[22] Swallow, Ph.D. thesis, Cambridge, 1954.
[23] Mackinnon and Waters, *J.*, 1953, 323.

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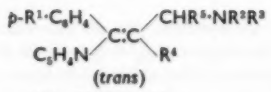
61. *Aminoalkyl Tertiary Carbinols and Derived Products. Part VI.*[1] *The Stereochemistry of Some* 1-*Phenyl*-1-2′-*pyridylprop*-1-*enes, and of Some* 3-(*Tertiary amino*)-1-*phenyl*-1-2′-*pyridylprop*-1-*enes carrying Additional Substituents.*

By D. W. Adamson, P. A. Barrett, J. W. Billinghurst, and T. S. G. Jones.

The spectra * of the *cis*- and *trans*-isomers of some 1-phenyl-1-2′-pyridylprop-1-enes resemble those of the corresponding 3-(tertiary amino)-compounds (VI) and (I).

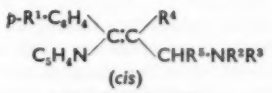
3-(Tertiary amino)-1-phenyl-1-2′-pyridylprop-1-enes carrying additional methyl or phenyl substituents have been prepared and separated into their geometrical isomers, and the latter have been assigned particular configurations. The spectra of the parent types (I) and (VI) are unaffected by the introduction of *meta*- or 3-substituents but are radically altered by *ortho*- or 2-substituents; the alterations are interpreted in terms of additional steric hindrance.

In Part V [1] we described the separation of a series of 3-(tertiary amino)-1-phenyl-1-2′-pyridylprop-1-enes into their *trans*- and *cis*-isomers (I) and (VI). The isomers were separated by displacement ion-exchange chromatography, the *trans*-isomer invariably being eluted first from the column. They differed significantly in their spectra,* the *cis*-isomers resembling styrene in giving a single peak in the neighbourhood of 250 mμ, and the *trans*-isomers resembling 2-vinylpyridine in giving two maxima, at *ca.* 240 and 280 mμ.



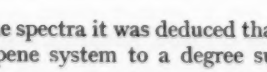
(*trans*)

(I): R^4, R^5 = H
(II): R^4 = Me, R^5 = H
(III): R^4 = Ph, R^5 = H
(IV): R^4 = H, R^5 = Me
(V): R^4 = H, R^5 = Ph

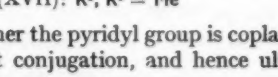


(*cis*)

(VI): R^4, R^5 = H
(VII): R^4 = Me, R^5 = H
(VIII): R^4 = Ph, R^5 = H
(IX): R^4 = H, R^5 = Me
(X): R^4 = H, R^5 = Ph



(XI): R^2 = Me, R^3 = H
(XII): R^2, R^3 = H
(XIII): R^2, R^3 = Me



(XIV): R^2 = Me, R^3 = H (*trans*)
(XV): R^2 = H, R^3 = Me (*cis*)
(XVI): R^2, R^3 = H
(XVII): R^2, R^3 = Me

From the spectra it was deduced that in the *trans*-isomer the pyridyl group is coplanar with the propene system to a degree sufficient to permit conjugation, and hence ultraviolet

* Throughout this paper " spectrum " is understood to mean ultraviolet absorption spectrum; *cis* and *trans* refer to the relation of the pyridyl and the (tertiary amino)methyl group.

[1] Adamson, Barrett, Billinghurst, and Jones, Part V, *J.*, 1957, 2315.

absorption of 2-vinylpyridine type, the phenyl group being forced out of the plane of the double bond by the steric effect of the aminomethyl group. A similar effect in the opposite sense determines the disposition of the *cis*-isomers.

We suggested that it was probably the methylene moiety of the aminomethyl group which effected this hindering and this has now been confirmed by the demonstration of similar spectral differences between isomers in which the tertiary amino-group is absent. The alcohols (XI; $R^1 = H$) and (XI; $R^1 = Cl$) gave, on dehydration, propenes which were separated by chromatography on alumina, or by ion-exchange chromatography, each into two isomers, one of each pair (XIV; $R^1 = H$ and Cl) showing (Fig. 1) the 2-vinylpyridine-like spectrum characteristic of the *trans*-isomers (I), and the other (XV; $R^1 = H$ and Cl) showing the styrene-like spectrum characteristic of the corresponding *cis*-isomers

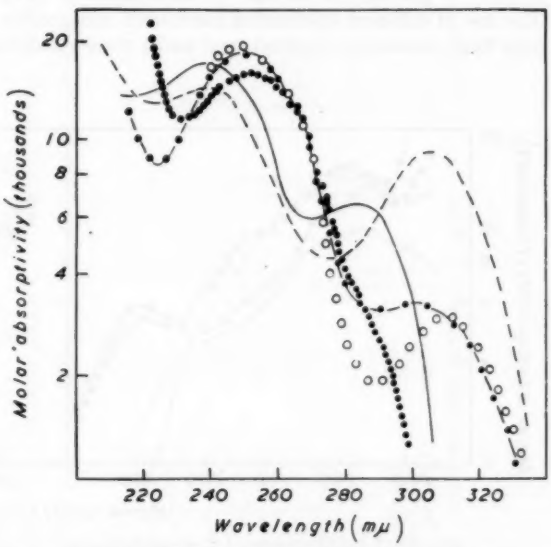
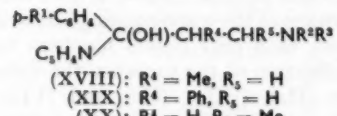
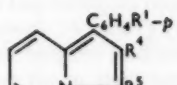


FIG. 1. trans-1-p-*Chlorophenyl*-1-2′-*pyridylprop*-1-*ene*:
—— *in* 0·1M-*ethanolic* NaOH;
– – – *in* 0·1M-*ethanolic* HCl.
cis-1-p-*Chlorophenyl*-1-2′-*pyridylprop*-1-*ene*:
. . . *in* 0·1M-*ethanolic* NaOH;
·—· *in* 0·1M-*ethanolic* HCl;
o o o *in* 5·5M-*aq.* HCl.

(VI). Both isomers show, in acid solution, the band at *ca.* 300 mμ characteristic of the *trans*-isomer (I) (ref. 1, Fig. 2, curve - - -) and of 2-vinylpyridine, but for (XV) it is much less intense than for (XIV). By analogy with the tertiary amino-isomers (I) and (VI), compounds (XIV) are designated *trans* and (XV) *cis*. In contrast with the tertiary amino-isomers, but in accordance with the pK_a values of their pyridyl nitrogen atoms,[2] the *cis*-propenes (XV) are eluted before the *trans*-propenes (XIV) in displacement ion-exchange chromatography. The corresponding phenylpyridylethylenes (XVI; $R^1 = H$ and Cl) prepared by dehydration of the alcohols (XII; $R^1 = H$ and Cl) were shown to be spectroscopically homogeneous by submission to ion-exchange or alumina chromatography. Their spectra (Fig. 2) were intermediate between those of the *trans*-isomers (I) and (XIV) and the *cis*-



(XVIII): $R^4 = Me$, $R_5 = H$
(XIX): $R^4 = Ph$, $R_5 = H$
(XX): $R^4 = H$, $R_5 = Me$
(XXI): $R^4 = H$, $R_5 = Ph$



(XXII)

isomers (VI) and (XV) in that they show (*a*) peaks at 230 and 235 mμ, (*b*) shoulders at 245 and 250 mμ, (*c*) a shelf at 280 mμ, and (*d*) a new peak at 300 mμ in acid solution.

[2] Everett and Jones, unpublished work.

XUM

We now describe geometrical isomers (II—V, VII—X) in which additional substituents are introduced into the parent types (I) and (VI) and assign them geometrical configurations, on the basis of their spectra where these retain the sharp distinction of those of the parent types. In those cases where substitution so alters the spectra as to make them inconclusive, two other criteria are employed, (i) the order of elution on ion-exchange chromatography, and (ii) the yield of the acetylpyrrocoline obtained on cyclisation. The *cis*-isomer (VI; $R^1 = Cl$, $NR^2R^3 = N < [CH_2]_4$) was shown [1] to cyclise on treatment with acetic anhydride to the acetylpyrrocoline (XXII; $R^1 = Cl$, $R^4 = H$, $R^5 = Ac$) under conditions which gave none from the *trans*-isomer (I), and this was offered as additional evidence of the correctness of the configurations assigned to these isomers. In Part VII (following paper) it is shown that cyclisation to the corresponding pyrrocoline (XXII) is general for all the *cis*-alkenylamines (VII—X) which have been examined. The use of different cyclisation conditions has greatly increased the yield of pyrrocoline over that previously reported, and under these conditions the corresponding *trans*-isomers

FIG. 2. FIG. 3.

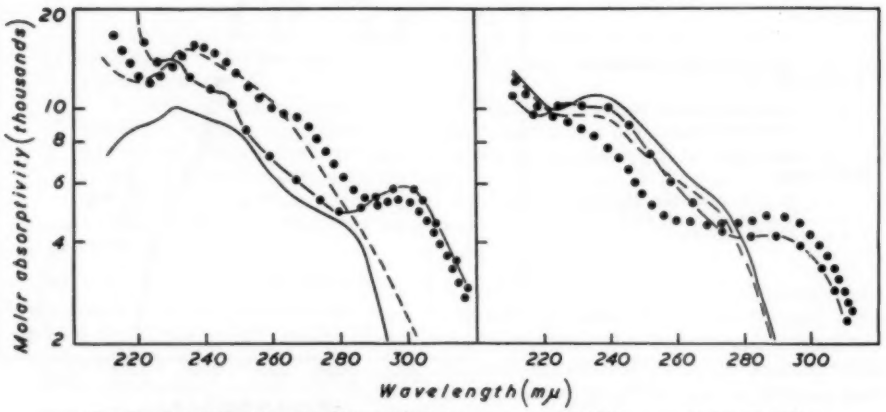


FIG. 2. 1-p-*Chlorophenyl*-1-2′-*pyridylethylene*: – – – *in* EtOH; . . . *in* 5M-*aq*. HCl. 1-*Phenyl*-1-2′-*pyridylethylene*: —— *in* EtOH; ·—· *in* 5M-*aq*. HCl.

FIG. 3. 2-*Methyl*-1-*phenyl*-1-2′-*pyridyl*-3-*pyrrolidinoprop*-1-*ene*: (*a*) trans, —— *in* EtOH; ·—· *in* 5M-*aq*. HCl; (*b*) cis, – – – *in* EtOH, . . . *in* 5M-*aq*. HCl.

(II—V) also give pyrrocoline. Where the configuration of the isomers is defined by their spectra the yield of pyrrocoline obtained from the *trans*- is, however, always lower than that from the *cis*-isomer under the same conditions. When the spectra are not diagnostic, we therefore assign the *cis*-configuration to that isomer which gives the higher yield of pyrrocoline. The cyclisation experiments, the results of which are assumed here, are described in the following paper.

2-Methyl Substituents.—Four 2-methyl-substituted alcohols (Table 2) (XVIII*a*, *b*, *c*, and *d*) have been prepared and dehydrated to mixtures of the corresponding alkenylamines (II) and (VII) (Table 4), from which, in all cases, each pure isomer has been isolated. Separation was best effected by fractional crystallisation of the oxalates, the differential solubility being high in all cases. The isomers (II*a*), (VII*a*), (II*c*), and (VII*c*) were further purified by crystallisation as their solid bases. The depression of melting point shown by these pairs of isomers, together with the fact that in each case the higher-melting base was derived from the lower-melting, more soluble, oxalate, established their purity. Separation by base-exchange chromatography, which was used [1] for separation of the parent isomers of types (I) and (VI), is of less value here because, as discussed below, the

TABLE 1. *Aryl 2-(tertiary amino)ethyl ketone hydrochlorides* $R^1 \cdot CO \cdot CH_2 \cdot CH_2 \cdot NR^2R^3, HCl$.

R^1	NR^2R^3	Yield (%)	M. p.[a]	Formula	Found (%)[b] C	H	N	Cl	Required (%) C	H	N	Cl
2-C_6H_4Me	$N<C_4H_8$	40	134—135°	$C_{14}H_{20}ONCl$	66·5	7·9	5·3	14·3	66·3	7·9	5·5	14·0
3-C_6H_4Me	$N<C_4H_8$	55	131—132 *	,,	—	—	5·6	14·3	—	—	5·5	14·0
4-C_6H_4Me	NMe_2	68	168 *	$C_{12}H_{18}ONCl$	63·3	7·9	5·9	15·8	63·3	7·9	6·2	15·6
,,	$N<C_4H_8$	49	170	$C_{14}H_{20}ONCl$	66·2	7·6	5·6	14·0	66·3	7·9	5·5	14·0
,,	$N<C_5H_{10}$	61	177—178	$C_{15}H_{22}ONCl$	67·6	8·0	5·2	13·5	67·3	8·2	5·2	13·3
2 : 4-$C_6H_3Me_2$	$N<C_4H_8$	47	150—152	$C_{15}H_{22}ONCl$	66·9	8·3	5·1	13·3	67·3	8·2	5·2	13·3
2 : 5-$C_6H_3Me_2$	$N<C_4H_8$	45	140—141	$C_{15}H_{22}ONCl$	66·8	8·0	5·2	13·4	67·3	8·2	5·2	13·3
3 : 4-$C_6H_3Me_2$	$N<C_4H_8$	60	169—170	$C_{15}H_{22}ONCl$	67·3	8·2	5·0	13·6	67·3	8·2	5·2	13·3
4-C_6H_4Et	$N<C_4H_8$	53	118—120 *	$C_{15}H_{22}ONCl$	67·4	8·3	5·0	13·4	67·3	8·2	5·2	13·3
4-$C_6H_4Pr^i$	$N<C_4H_8$	57	167—168	$C_{16}H_{24}ONCl$	—	—	4·8	12·8	—	—	5·0	12·6
4-$C_6H_4Bu^t$	$N<C_4H_8$	60	157—158	$C_{17}H_{26}ONCl$	68·9	8·7	4·7	12·3	69·0	8·8	4·7	12·0

[a] After crystalln. from ethanol–ethyl acetate. With decomp. except those marked *. [b] Analytical samples were dried at 100° *in vacuo*.

TABLE 2. *1-Aryl-1-2′-pyridylalkan-1-ols and 3-(tertiary amino)-1-aryl-1-2′-pyridylalkan-1-ols.*

Compound	R^1	R^2R^3	M. p.	Formula	Found (%) C	H	N	Cl	Required (%) C	H	N	Cl
XI*b*	Cl	H,Me	65°[a]	$C_{14}H_{14}ONCl$	67·9	5·8	6·0	13·4	67·9	5·7	5·7	14·3
XIII*a*	H	Me,Me	67—69[a]	$C_{15}H_{17}ON$	78·8	7·5	—	—	79·3	7·5	—	—
XIII*b*	Cl	,,	115[a]	$C_{15}H_{16}ONCl$	68·8	6·1	—	13·7	68·9	6·1	—	13·6
XVIII*a*	H	$<[CH_2]_5$	134	$C_{20}H_{26}ON_2$	77·4	8·1	9·4	—	77·4	8·4	9·0	—
XVIII*b*	Cl	,,	121	$C_{20}H_{25}ON_2Cl$	69·8	7·3	8·0	10·0	69·7	7·3	8·1	10·3
XVIII*c*	H	$<[CH_2]_4$	111	$C_{19}H_{24}ON_2$	77·3	8·1	9·6	—	77·0	8·1	9·5	—
XVIII*d*	Cl	,,	102	$C_{19}H_{23}ON_2Cl$	69·2	7·0	8·5	10·8	69·0	7·0	8·5	10·7
XIX*a*	H	$<[CH_2]_5$	146	$C_{25}H_{26}ON_2$	80·3	7·5	7·5	—	80·7	7·5	7·5	—
XIX*b*	Cl	$<[CH_2]_4$	158	$C_{24}H_{23}ON_2Cl$	73·4	6·4	7·0	8·7	73·4	6·4	7·1	9·0
XX*a*	H	$<[CH_2]_5$	86	$C_{20}H_{26}ON_2$	77·3	8·0	8·7	—	77·4	8·4	9·0	—
XX*b*	H	$<[CH_2]_4$	83[a]	$C_{19}H_{24}ON_2$	77·0	8·0	9·3	—	77·0	8·1	9·5	—
XX*c*	Cl	,,	106 *[a]	$C_{19}H_{23}ON_2Cl$	68·5	6·8	8·4	10·5	69·0	7·0	8·5	10·7
,,	,,	,,	117 *[a]	,,	68·8	6·9	8·4	10·3	,,	,,	,,	,,
XXI*a*	H	$<[CH_2]_5$	124	$C_{25}H_{28}ON_2$	80·6	7·7	7·6	—	80·7	7·5	7·5	—
XXIX*a*	H	$<[CH_2]_5$	81[a]	$C_{19}H_{24}ON_2$	77·0	7·8	9·3	—	77·0	8·1	9·5	—
XXIX*b*	Cl	,,	115	$C_{19}H_{23}ON_2Cl$	68·7	7·1	8·2	10·7	69·0	7·0	8·5	10·7

[a] Solvent light petroleum (b. p. 40—60°). Others from light petroleum (b. p. 60—80°). * Diastereoisomers (see text).

TABLE 3. 3-(*Tertiary amino*)-1-*aryl*-1-2′-*pyridylpropan*-1-*ols* (XXIII) *and* (XXIV).

Compound	R^1	R^4	R^5	NR^2R^3	Yield (%)	Derivative	M. p.[b]	Solvent for recrystn.	Formula	Found (%) C	Found (%) H	Found (%) N	Required (%) C	Required (%) H	Required (%) N
XXIII*a*	H	H	Me	N<C_4H_8	53	Base	106—107°	EtOH	$C_{19}H_{24}ON_2$	76·7	8·0	9·3	77·0	8·1	9·5
						Oxalate	181—182	MeOH	$C_{21}H_{26}O_5N_2$	65·1	6·7	—	65·3	6·7	—
XXIV*a*	H	Me	H	N<C_4H_8	56	Base	54—55	[c]	$C_{19}H_{24}ON_2$	77·2	8·2	9·5	77·0	8·1	9·5
						Oxalate	155—156	EtOH	$C_{21}H_{26}O_5N_2$	65·4	6·5	—	65·3	6·7	—
XXIV*b*	Me	H	H	NMe_2	60	Base	86—87	EtOH	$C_{17}H_{22}ON_2$	75·5	8·0	10·2	75·6	8·1	10·4
						Oxalate	163—164	MeOH	$C_{19}H_{24}O_5N_2$	63·3	6·5	—	63·3	6·7	—
XXIV*c*	Me	H	H	N<C_4H_8	80	Base	119—120	EtOH	$C_{19}H_{24}ON_2$	77·0	7·8	9·4	77·0	8·1	9·5
						Oxalate	148—119	EtOH–EtOAc	$C_{21}H_{26}O_5N_2$	65·3	6·8	—	65·3	6·7	—
XXIV*d*	Me	H	H	N<C_5H_{10}	54	Base	85—86	EtOH	$C_{20}H_{26}ON_2$	77·7	8·3	9·0	77·4	8·4	9·0
						Oxalate	146—147	MeOH	$C_{22}H_{28}O_5N_2$	65·6	6·9	—	66·0	7·0	—
XXIII*b*	Me	H	Me	N<C_4H_8	69	Base	111—112	EtOH	$C_{20}H_{26}ON_2$	77·2	8·5	9·3	77·4	8·4	9·0
						Oxalate	175—176	MeOH	$C_{22}H_{28}O_5N_2$	65·9	6·8	—	66·0	7·0	—
XXIII*c*	H	Me	Me	N<C_4H_8	58	Base	107—108	EtOH	$C_{20}H_{26}ON_2$	77·3	8·4	8·7	77·4	8·4	9·0
						Oxalate [a]	196	MeOH	$C_{23}H_{30}O_5N_2$	62·2	6·6	—	62·0	6·5	—
XXIV*e*	Me	Me	H	N<C_4H_8	67	Base	104—105	EtOH	$C_{20}H_{26}ON_2$	76·9	8·4	8·9	77·4	8·4	9·0
						Oxalate	142—143	EtOH	$C_{22}H_{28}O_5N_2$	66·0	6·8	—	66·0	7·0	—
XXIV*f*	Et	H	H	N<C_4H_8	65	Base	112—113	EtOH	$C_{20}H_{26}ON_2$	77·4	8·4	9·0	77·4	8·4	9·0
						Oxalate	147—149	EtOH	$C_{22}H_{28}O_5N_2$	65·8	6·9	—	66·0	7·0	—
XXIV*g*	Pr[i]	H	H	N<C_4H_8	74	Base	83—84	EtOH	$C_{21}H_{28}ON_2$	77·4	8·5	8·8	77·8	8·6	8·6
						Oxalate	146—147	EtOH–EtOAc	$C_{23}H_{30}O_5N_2$	66·8	7·1	—	66·7	7·2	—
XXIV*h*	Bu[t]	H	H	N<C_4H_8	80	Base	120—121	EtOH	$C_{22}H_{30}ON_2$	78·1	8·8	7·9	78·1	8·9	8·3
						Oxalate	127—128	$CHCl_3$–EtOAc	$C_{24}H_{32}O_5N_2$	67·1	7·6	—	67·3	7·5	—

[a] Sesquioxalate. [b] The oxalates melted with decomp. [c] Light petroleum (b. p. <40°).

TABLE 4. 1-*Aryl*-1-2′-*pyridylalk*-1-*ene and* 3-(*tertiary amino*)-1-*aryl*-1-2′-*pyridylalk*-1-*ene isomers* (cf. Table 4a).

TABLE 4. 1-*Aryl*-1-2′-*pyridylalk*-1-*ene and* 3-(*tertiary amino*)-1-*aryl*-1-2′-*pyridylalk*-1-*ene isomers* (cf. Table 4*a*).

Compound	R¹	R²R³	Isomer	Derivative	M. p. or b. p./mm.	Ultraviolet absorption max.[a] Base[d] λ		$10^{-3}\varepsilon$		Salt[e] λ		$10^{-3}\varepsilon$		Cation[f] λ		$10^{-3}\varepsilon$	
XVI*a*	H	H,H	—	Base	120—122°/0·5	232	*275*	9·8	*4·9*	—	—	—	—	230	300	13·8	5·9
,,	,,	,,	—	Hydrochloride	186—187[a]	—	—	—	—	—	—	—	—	—	—	—	—
XVI*b*	Cl	H,H,	—	Hydrochloride	192—193[b]	232	—	16·2	—	—	—	—	—	237	297	15·6	5·4
XIV*a*	H	H,Me	*trans*	Hydrochloride	138[a]	242	286	12·6	5·9	—	—	—	—	242	303	11·3	6·6[g]
XV*a*	,,	,,	*cis*	Base	110/0·5	244	—	13·7	—	—	—	—	—	241	304	14·9	3·4[g]
XIV*b*	Cl	,,	*trans*	Hydrochloride	197—199	240	286	17·9	6·4	—	—	—	—	240	307	14·6	9·3[g]
XV*b*	,,	,,	*cis*	Base	150—152/0·5	253	—	16·0	—	—	—	—	—	248	300	15·3	3·4[g]
XVII*a*	H	Me,Me	—	Base	126—128/0·5	241	*270*	11·2	*5·0*	—	—	—	—	234	305	10·7	4·8[g]
XVII*b*	Cl	,,	—	Base	150—152/0·5	245	—	14·1	—	—	—	—	—	244	310	15·0	5·7
II*a*	H	<[CH₂]₅	*trans*	Base	85—86	230	*265*	10·1	*5·8*	225	*270*	10·7	*5·6*	—	—	—	—
,,	,,	,,	*trans*	Oxalate	175—176	—	—	—	—	—	—	—	—	—	—	—	—
VII*a*	,,	,,	*cis*	Base	100—102	240[c]	*270*	11·2	*4·7*	225	*268*	20·0	*7·9*	—	—	—	—
,,	,,	,,	*cis*	Oxalate	125	—	—	—	—	—	—	—	—	—	—	—	—
II*b*	Cl	,,	*trans*	Oxalate	201—202	—	—	—	—	240	283	13·0	5·8	—	—	—	—
VII*b*	,,	,,	*cis*	Oxalate	75—77	—	—	—	—	232	—	13·4	—	—	—	—	—
II*c*	H	<[CH₂]₄	*trans*	Base	55	235	*265*	9·8	*5·8*	—	—	—	—	*230*	290	*9·0*	4·8
,,	,,	,,	*trans*	Oxalate	158—159	—	—	—	—	—	—	—	—	—	—	—	—
VII*c*	,,	,,	*cis*	Base	69—70	237	*270*	11·1	*6·0*	—	—	—	—	235	290	10·5	4·3
II*d*	Cl	,,	*trans*	Oxalate	216	238	—	10·2	—	231	—	14·0	—	232	*290*	14·1	*5·7*
VII*d*	,,	,,	*cis*	Oxalate	134—135	246	—	14·0	—	235	*280*	15·5	7·2	242	*290*	15·6	*7·6*
III*a* or VIII*a*	H	<[CH₂]₅	—	Base	91—92	270	—	10·0	—	—	—	—	—	244	—	13·0	—
III*b*	Cl	<[CH₂]₄	*trans*	Base	104—105	231	259	15·6	11·1	—	—	—	—	240	*295*	14·7	*9·1*
,,	,,	,,	*trans*	Oxalate	151—152	—	—	—	—	—	—	—	—	—	—	—	—
VIII*b*	,,	,,	*cis*	Base	110	240	*280*	14·8	*11·9*	—	—	—	—	243	*310*	17·0	*4·3*
,,	,,	,,	*cis*	Oxalate	147—148	—	—	—	—	—	—	—	—	—	—	—	—
IV*a*	H	<[CH₂]₅	*trans*	Base	—	240	*282*	13·0	*6·0*	—	—	—	—	—	—	—	—
IX*a*	,,	,,	*cis*	Base	—	248	—	11·2	—	—	—	—	—	—	—	—	—
IV*b*	,,	<[CH₂]₄	*trans*	Base	—	—	—	—	—	—	—	—	—	240	282	12·1	6·2
IX*b*	,,	,,	*cis*	Base	—	—	—	—	—	—	—	—	—	245	—	12·5	—
IV*c*	Cl	,,	*trans*	Base	—	—	—	—	—	233	262	16·0	7·4	—	—	—	—
,,	,,	,,	*trans*	Oxalate	159—160	—	—	—	—	—	—	—	—	—	—	—	—
IX*c*	,,	,,	*cis*	Base	200—204/0·3	—	—	—	—	245	—	16·0	—	—	—	—	—
X*a*	H	<[CH₂]₅	*cis*	Base	77—79	253	—	17·9	—	—	—	—	—	255	*291*	14·0	*3·84*
XXX*a*	,,	<[CH₂]₄	*trans*	Oxalate	158—160	250	—	13·5	—	—	—	—	—	260	—	14·0	—
XXXI*a*	,,	,,	*cis*	Oxalate	152	242	255	11·2	11·2	—	—	—	—	250	—	10·0	—
XXX*b*	Cl	,,	*trans*	Oxalate	140—141	260	—	15·5	—	—	—	—	—	217	265	14·0	18·0
XXXI*b*	,,	,,	*cis*	Oxalate	175—176	250	—	11·9	—	—	—	—	—	217	265	14·0	12·0

[a] From chloroform–ether. [b] From chloroform–ethyl acetate. [c] Values italicised are for inflexions and are approximate. [d] Base dissolved in EtOH, or salt made alkaline in EtOH. [e] Salt dissolved in EtOH. [f] Salt or base dissolved in 5N-HCl, except [g] where solvent was 0·1N-HCl in EtOH.

ultraviolet spectra of these isomers are so nearly identical as to be useless for controlling the progress of the separation. The method was used for examples (*a*) and (*c*) in which both isomeric bases were solid, and determination of mixed m. p.s of the fractions gave a satisfactory, if tedious, control of the separation. The isomer giving the sparingly soluble oxalate was eluted first on ion-exchange chromatography and that giving the more soluble oxalate gave a substantially higher yield of pyrrocoline. The *trans*-configuration (II) is therefore assigned to the former and the *cis*-configuration (VII) to the latter isomer in each case. The isomers (II) and (VII) differ from the parent types (I) and (VI) in that their spectra are almost identical (Fig. 3) and take the form of a rather broad curve with a single peak at *ca.* 240 mμ, showing a distinct shoulder at 270 mμ. In acid solution, both isomers give a peak at 290 mμ. The form of the curves, being a hybrid of those of styrene and 2-vinylpyridine, and their similarity, are readily interpreted in steric terms. The presence of the 2-methyl group in (II) and (VII) in addition to the aminomethyl group introduces a steric symmetry lacking in (I) and (VI). It is to be expected that in each isomer both aryl groups, being equally hindered, have an equal opportunity to attain the necessary degree of co-planarity and will contribute equally to the spectrum.

TABLE 4*a*.

Compound	Constitution	Found (%) C	H	N	Cl	Required (%) C	H	N	Cl
XVI*a*	$C_{13}H_{11}N$	85·8	5·6	7·7	—	86·2	6·1	7·7	—
,,	$C_{13}H_{11}N,HCl$	71·4	5·6	6·1	—	71·7	5·5	6·4	—
XVI*b*	$C_{13}H_{10}NCl,HCl$	62·3	4·4	5·6	27·8	61·9	4·4	5·6	28·2
XIV*a*	$C_{14}H_{13}N,HCl$	72·0	5·8	6·0	15·6	72·6	6·0	6·0	15·3
XV*a*	$C_{14}H_{13}N$	86·0	6·6	7·0	—	86·2	6·7	7·2	—
XIV*b*	$C_{14}H_{12}NCl,HCl$	63·7	4·9	—	26·9	63·2	4·9	—	26·7
XV*b*	$C_{14}H_{12}NCl$	72·6	5·4	5·6	15·6	73·2	5·2	6·1	15·5
XVII*a*	$C_{15}H_{15}N$	85·9	7·2	6·6	—	86·1	7·2	6·7	—
XVII*b*	$C_{15}H_{14}NCl$	73·0	5·8	5·7	14·5	73·9	5·7	5·7	14·6
II*a*	$C_{26}H_{24}N_2$	81·8	8·0	9·9	—	82·2	8·2	9·6	—
,,	$C_{26}H_{24}N_2,C_2H_2O_4$	69·0	7·0	7·2	—	69·1	6·8	7·3	—
VII*a*	$C_{26}H_{24}N_2$	82·1	8·1	9·4	—	82·2	8·2	9·6	—
,,	$C_{26}H_{24}N_2,C_2H_2O_4$	68·8	7·1	7·3	—	69·1	6·8	7·3	—
II*b*	$C_{26}H_{23}N_2Cl,C_2H_2O_4$	63·2	6·0	6·5	8·5	63·4	6·0	6·7	8·5
VII*b*	$C_{26}H_{23}N_2Cl,C_2H_2O_4$	62·9	6·2	—	8·5	63·4	6·0	6·7	8·5
II*c*	$C_{19}H_{22}N_2$	81·5	7·4	10·2	—	82·0	7·9	10·1	—
,,	$C_{19}H_{22}N_2,C_2H_2O_4$	68·3	6·4	7·5	—	68·5	6·5	7·6	—
VII*c*	$C_{19}N_{22}N_2$	81·4	7·7	11·1	—	82·0	7·9	10·1	—
II*d*	$C_{19}H_{21}N_2Cl,C_2H_2O_4$	62·6	5·7	7·0	8·9	62·6	5·7	7·0	8·8
VII*d*	$C_{19}H_{21}N_2Cl,C_2H_2O_4$	62·2	5·7	6·9	9·0	62·6	5·7	7·0	8·8
III*a* or VIII*a*	$C_{25}H_{26}N_2$	84·7	7·3	7·7	—	84·7	7·3	7·9	—
III*b*	$C_{24}H_{23}N_2Cl$	76·5	5·9	7·6	9·6	76·9	6·1	7·5	9·5
,,	$C_{24}H_{23}N_2Cl,C_2H_2O_4$	67·5	5·5	6·1	7·2	67·2	5·4	6·0	7·6
VIII*b*	$C_{24}H_{23}N_2Cl$	76·9	6·2	7·5	9·5	76·9	6·1	7·5	9·5
,,	$C_{24}H_{23}N_2Cl,C_2H_2O_4$	67·3	5·4	6·2	7·6	67·2	5·4	6·0	7·6
IV*a*	$C_{20}H_{24}N_2$	81·9	8·1	9·4	—	82·2	8·2	9·6	—
IX*a*	$C_{20}H_{24}N_2$	82·0	7·6	9·3	—	82·2	8·2	9·6	—
IV*b*	$C_{19}H_{22}N_2$	81·7	7·9	10·0	—	82·0	7·9	10·1	—
IX*b*	$C_{19}H_{22}N_2$	81·9	7·7	10·2	—	82·0	7·9	10·1	—
IV*c*	$C_{19}H_{21}N_2Cl$	73·1	6·5	8·7	11·5	73·0	6·7	9·0	11·4
,,	$C_{19}H_{21}N_2Cl,1\frac{1}{2}C_2H_2O_4$	58·7	5·4	6·2	7·9	59·0	5·4	6·3	7·9
IX*c*	$C_{19}H_{21}N_2Cl$	72·5	6·7	8·8	11·5	73·0	6·7	9·0	11·4
X*a*	$C_{25}H_{26}N_2$	84·8	7·4	7·9	—	84·7	7·3	7·9	—
XXX*a*	$C_{19}H_{22}N_2,C_2H_2O_4$	68·0	6·4	7·7	—	68·5	6·5	7·6	—
XXXI*a*	$C_{19}H_{22}N_2,C_2H_2O_4$	68·2	6·5	7·6	—	68·5	6·5	7·6	—
XXX*b*	$C_{19}H_{21}N_2Cl,C_2H_2O_4$	62·8	6·1	6·4	8·5	62·6	5·7	7·0	8·8
XXXI*b*	$C_{19}H_{21}N_2Cl,C_2H_2O_4$	62·5	6·0	6·6	8·6	62·6	5·7	7·0	8·8

The spectra of the non-aminated *iso*butenes (XVII; R^1 = H and Cl) are similar to those of the isomers (II) and (VII), and consist of single bands with peaks at 242 and 246 mμ respectively and only slight indication of submerged peaks at 270 mμ. In acid solution they show well-defined peaks at 320 mμ.

2-*Phenyl Substituents.*—Two 2-phenyl-substituted alcohols (Table 2) (XIX*a* and *b*)

TABLE 5. 3-(*Tertiary amino*)-1-*aryl*-1-2'-*pyridylprop*-1-*enes* (XXV), (XXVII), (XXVI), and (XXVIII) (cf. Table 5*a*). -

Compound	R¹	R⁴	R⁵	NR^2R^3	Deriv.	M. p.[a]	Solvent for recrystn.	Ultraviolet absorption max.[c] Salt in EtOH λ		$10^{-3}\varepsilon$		Cation in H_2O[d] λ		$10^{-3}\varepsilon$		Base in EtOH[e] λ		$10^{-3}\varepsilon$	
XXV*a*	H	H	Me	N<C_4H_8	Oxalate	160—161°	EtOH	237	281	13·7	7·3	237	294	9·0	11·0	240	288	13·2	6·0
XXVII*a*	,,	,,	,,	,,	Oxalate	169—170	EtOH	231	277	11·8	5·9	270	290	6·8	6·1	233	277	13·0	5·2
XXVI*a*	H	Me	H	N<C_4H_8	Oxalate	147—148	EtOH	241	282	14·0	8·6	—	—	—	—	238	284	14·4	7·3
XXVIII*a*	,,	,,	,,	,,	Oxalate	182—183	MeOH	250	*282*	12·0	*6·0*	—	—	—	—	250	—	13·7	—
XXVI*b*	Me	H	H	NMe_2	Oxalate	173—174	EtOH	235	280	13·3	7·0	—	—	—	—	—	—	—	—
XXVIII*b*	,,	,,	,,	,,	Oxalate	181—182	MeOH	234	260	13·4	12·3	—	—	—	—	—	—	—	—
XXVI*c*	Me	H	H	N<C_4H_8	Base	59—61 *	Pet †	—	—	—	—	—	—	—	—	236	285	15·3	6·8
,,	,,	,,	,,	,,	Oxalate	173—174	MeOH	233	283	16·2	8·2	—	—	—	—	238	285	12·5	5·8
,,	,,	,,	,,	,,	HCl[b]	116—118 *	H_2O	235	283	15·0	7·4	—	—	—	—	—	—	—	—
,,	,,	,,	,,	,,	HBr[b]	119—121 *	H_2O	230	275	15·5	8·1	—	—	—	—	—	—	—	—
XXVIII*c*	,,	,,	,,	,,	Oxalate	149—150 *	EtOH	233	260	13·6	13·8	—	—	—	—	252	—	14·0	—
XXVI*d*	Me	H	H	N<C_5H_{10}	Oxalate	164—165	MeOH	233	283	13·0	6·0	292	—	9·0	—	237	285	12·0	5·2
XXVIII*d*	,,	,,	,,	,,	Oxalate	167—169	EtOH	262	—	13·5	—	255	—	16·0	—	250	—	13·0	—
XXV*b*	Me	H	Me	N<C_4H_8	Oxalate	168—169	EtOH	237	281	15·0	8·1	290	—	9·0	—	*235*	*280*	*11·5*	*5·4*
XXVII*b*	,,	,,	,,	,,	Oxalate	175—176	EtOH	230	273, 281	16·0	8·4, 8·1	—	—	—	—	238	285	12·1	6·4
XXV*c*	H	Me	Me	N<C_4H_8	Oxalate	156—157	EtOH	237	282	13·8	8·0	235	295	8·2	11·0	242	284	13·0	8·0
XXVII*c*	,,	,,	,,	,,	Oxalate	176—177	EtOH	235	*280*	12·5	*6·9*	270	*290*	6·6	*5·8*	232	271	12·0	6·4
XXVI*e*	Me	Me	H	N<C_4H_8	Oxalate	160—161	EtOH	235	281	16·1	8·3	—	—	—	—	238	282	14·5	7·0
XXVIII*e*	,,	,,	,,	,,	Base	57—58 *	Pet †	—	—	—	—	—	—	—	—	252	—	14·8	—
,,	,,	,,	,,	,,	Oxalate	174—175	EtOH	*235*	261	*14·5*	13·5	—	—	—	—	254	—	14·4	—
XXVI*f*	Et	H	H	N<C_4H_8	Oxalate	153—154	EtOH–EtOAc	235	282	12·0	5·5	—	—	—	—	—	—	—	—
XXVI*g*	*i*-Pr	H	H	N<C_4H_8	Oxalate	166—167	EtOH–EtOAc	235	282	12·1	5·7	—	—	—	—	235	285	14·0	6·4
XXVIII*g*	,,	,,	,,	,,	Oxalate	168	EtOH–EtOAc	235	260	14·0	14·0	—	—	—	—	260	—	15·0	—
XXVI*h*	*t*-Bu	H	H	N<C_4H_8	Oxalate	164	EtOH–EtOAc	230	280	13·6	6·6	—	—	—	—	237	283	12·5	5·2
XXVIII*h*	,,	,,	,,	,,	Oxalate	174	EtOH–EtOAc	235	262	15·0	15·0	—	—	—	—	240	—	11·3	—

[a] With decomp. except those marked *. [b] Monohydrate: the analytical sample was dried at 100° *in vacuo*. [c] Values italicised are for inflexions and are approximate. [d] Base or salt dissolved in aq. HCl (0·1N or stronger). [e] Base dissolved in EtOH or salt dissolved in EtOH containing 0·1N-NaOH.
† Light petroleum (b. p. 40—60°).

have been prepared and dehydrated to mixtures of the alkenylamines (III) and (VIII) (Table 4). The alcohol (XIX*b*) gave on dehydration a mixture of alkenylamines from which two pure solid isomers (III*b*) and (VIII*b*) were isolated by ion-exchange chromatography, controlled by the m. p.s and mixed m. p.s of the fractions. The isomers were also separated, less satisfactorily, by fractional crystallisation of the oxalates. The yield of pyrrocoline from the isomer which was eluted first was lower than from that eluted second. The former is therefore assigned the *trans*- and the latter the *cis*-configuration. The spectra of the diphenylpropenes (III*b*) and (VIII*b*) are similar and, except for some extension towards the red, resemble the *trans*-alkenylamine type: both show the characteristic absorption at 300—320 mμ in acid solution, the *trans*-isomer absorbing the more intensely.

The alcohol (XIX*a*) gave, on dehydration, a semi-solid mixture from which one solid isomer (III*a*) or (VIII*a*) has been isolated by crystallisation and by base-exchange chromatography. The later fractions of the column gave oil which presumably consisted substantially of the second isomer. However, as both the solid and the liquid fractions gave approximately equal yields of pyrrocoline, there are insufficient grounds for assigning configurations.

3-*Methyl Substituents.*—Three 3-methyl-substituted alcohols [Table 2; (XX*a*), (XX*b*), and (XX*c*)] have been prepared and dehydrated to mixtures, each of which was separated by base-exchange chromatography into the *trans*- and the *cis*-alkenylamines (IV) and (IX). As expected, their absorption spectra resembled those of the unsubstituted types (I) and (VI) and served to control the separations.

TABLE 5*a*.

		Found (%)			Required (%)		
Compound	Formula	C	H	N	C	H	N
XXV*a*	$C_{21}H_{24}O_4N_2$	68·3	6·3	7·6	68·5	6·5	7·6
XXVII*a*	$C_{21}H_{24}O_4N_2$	68·1	6·2	7·4	68·5	6·5	7·6
XXVI*a*	$C_{21}H_{24}O_4N_2$	68·8	6·7	7·8	68·5	6·5	7·6
XXVIII*a*	$C_{21}H_{24}O_4N_2$	68·5	6·4	7·6	68·5	6·5	7·6
XXVI*b*	$C_{19}H_{22}O_4N_2$	66·9	6·2	8·2	66·7	6·4	8·2
XXVIII*b*	$C_{19}H_{22}O_4N_2$	66·8	6·4	8·2	66·7	6·4	8·2
XXVI*c*	$C_{19}H_{22}N_2$	—	—	9·9	—	—	10·1
,,	$C_{21}H_{24}O_4N_2$	68·5	6·2	7·6	68·5	6·5	7·6
,,	$C_{19}H_{23}N_2Cl$	—	—	11·3 •	—	—	11·3 •
,,	$C_{19}H_{23}N_2Br$	—	—	22·0 •	—	—	22·3 •
XXVIII*c*	$C_{21}H_{24}O_4N_2$	68·2	6·3	7·4	68·5	6·5	7·6
XXVI*d*	$C_{23}H_{26}O_4N_2$	69·2	6·8	7·2	69·1	6·8	7·3
XXVIII*d*	$C_{23}H_{26}O_4N_2$	69·2	6·8	7·5	69·1	6·8	7·3
XXV*b*	$C_{23}H_{26}O_4N_2$	69·1	6·8	7·3	69·1	6·8	7·3
XXVII*b*	$C_{23}H_{26}O_4N_2$	68·8	7·0	7·1	69·1	6·8	7·3
XXV*c*	$C_{23}H_{26}O_4N_2$	69·2	6·8	7·3	69·1	6·8	7·3
XXVII*c*	$C_{23}H_{26}O_4N_2$	68·6	6·7	7·1	69·1	6·8	7·3
XXVI*e*	$C_{23}H_{26}O_4N_2$	69·0	7·0	7·3	69·1	6·8	7·3
XXVIII*e*	$C_{20}H_{24}N_2$	82·2	8·2	9·6	82·2	8·2	9·6
,,	$C_{23}H_{26}O_4N_2$	68·9	6·9	7·3	69·1	6·8	7·3
XXVI*f*	$C_{23}H_{26}O_4N_2$	68·8	6·8	7·2	69·1	6·8	7·3
XXVI*g*	$C_{23}H_{28}O_4N_2$	69·6	6·9	6·9	69·7	7·1	7·1
XXVIII*g*	$C_{23}H_{28}O_4N_2$	69·8	6·9	6·8	69·7	7·1	7·1
XXVI*h*	$C_{24}H_{30}O_4N_2$	69·7	7·3	6·6	70·2	7·3	6·8
XXVIII*h*	$C_{24}H_{30}O_4N_2$	70·2	6·9	6·7	70·2	7·3	6·8

• Halogen analysis.

3-*Phenyl Substituents.*—The 3-phenyl alcohol (XXI*a*) (Table 2) showed unusual lability to sulphuric acid, perhaps associated with the fact that the compound is a substituted benzylamine, and did not survive dehydration under any but the mildest conditions. It was perhaps a consequence of this that the derived alkenylamine (X*a*) (Table 4) was found on ion-exchange chromatography to contain only *cis*-isomer. The *trans*-isomer has not been prepared. The configuration of the *cis*-isomer is defined by its styrene-like

spectrum and confirmed by the high yield of 1 : 3-diphenylpyrrocoline obtained on ring closure.

Methyl Substituents in the Phenyl Group.—Three alcohols [Table 3; (XXIII*a*), (XXIII*b*), and (XXIII*c*)] containing an *o*-methyl substituent in the phenyl group have been prepared and on dehydration gave mixtures which were separated by base-exchange chromatography into the isomeric alkenylamines (XXV) and (XXVII) (Table 5). In each case the spectrum (Fig. 4) of the *trans*-isomer (XXV) is of normal vinylpyridine type. The spectrum of the *cis*-isomer (XXVII) shows little trace of the styryl type of absorption, but only a broad shelf (ε ~5000) in the 260—280 mμ region. In this isomer, in addition to the normal hindering of the pyridyl group by the aminomethylene group, the hindering effect of the *o*-methyl group is so considerable that the phenyl group too is prevented from conjugating efficiently with the double bond. The spectrum is therefore a hybrid one though closer to the vinylpyridine than to the styrene type. In acid solution, a typical peak at 300 mμ is given by the *trans*-isomer and a lower, broader shelf by the *cis*-form.

The configurations of the isomers to which the spectra are referred are confirmed by the

FIG. 4. FIG. 5.

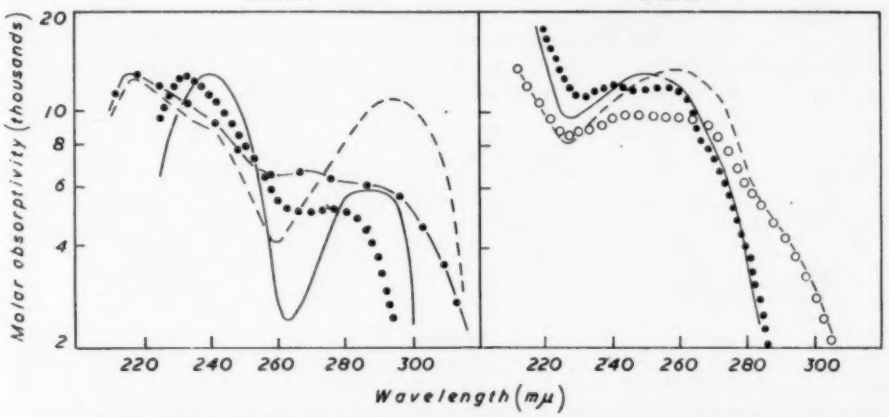


FIG. 4. 1-2′-*Pyridyl*-3-*pyrrolidino*-1-*o*-*tolylprop*-1-*ene oxalate*: (*a*) trans, —— *in* 0·1M-*ethanolic* NaOH, – – – *in* 5M-*aq.* HCl; (*b*) cis, . . . *in* 0·1M-*ethanolic* NaOH, ·—· *in* 5M-aq. HCl.

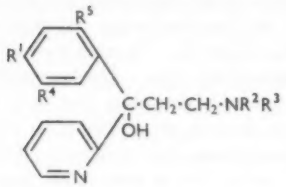
FIG. 5. 1-(3-*Methyl*-2-*pyridyl*)-1-*phenyl*-3-*pyrrolidinoprop*-1-*ene oxalate*: (*a*) trans, . . . *in* 0·1M-*ethanolic* NaOH, o o o *in* 5M-*aq.* HCl; (*b*) cis, —— *in* 0·1M-*ethanolic* NaOH, – – – *in* 5M-*aq.* HCl.

order of elution and by cyclisation experiments which were unusually conclusive in that the *cis*-isomer gave a high yield of pyrrocoline and the *trans*-isomer gave none.

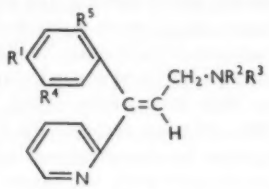
Several alcohols [Table 3; (XXIV)] carrying *m*- or *p*-alkyl substituents in the phenyl group have been prepared and dehydrated to the corresponding alkenylamines, and the isomers (Table 5) separated by ion-exchange chromatography. As expected, the isomers (XXVI) and (XXVIII) showed ultraviolet absorption spectra resembling those of the parent types (I) and (VI).

Picolylalkenylamines.—Two (3-picolyl)carbinols [Table 2; (XXIX*a*) and (XXIX*b*)] have been prepared and dehydrated to mixtures, each of which was separated by fractional crystallisation of the oxalates into the isomeric alkenylamines (XXX) and (XXXI) (Table 4). The pattern of their spectra (Fig. 5) is the reverse of that discussed above for the *o*-tolyl isomers (XXV) and (XXVII). The spectrum of the *cis*-isomer is of normal styrene type, and that of the *trans*-isomer is of modified styrene type, taking the form of a broad, flattened peak extending from 240 to 260 mμ, but showing traces of the vinylpyridine absorption—a peak at 240 mμ and a shoulder at 280 mμ of relatively high (ε ~8000) intensity. In acid solution, both isomers give spectra of the *cis*-type—a low

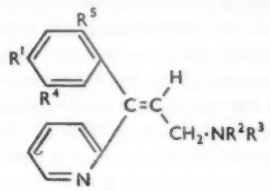
shoulder in the 300 mμ region (ref. 1, Fig. 2, curve – · – · –). The spectra of the *trans*-isomers are interpreted as showing that the hindering effect of the 3-methyl substituent is so considerable that, despite the presence of the *cis*-aminomethyl group, it is easier for



(XXIII) : R^5 = Me
(XXIV) : R^5 = H



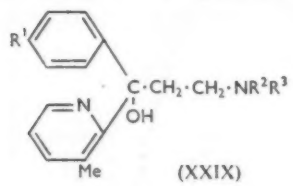
(XXV) : R^5 = Me
(XXVI) : R^5 = H



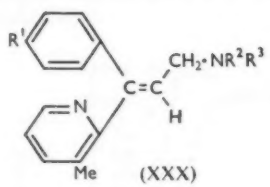
(XXVII) : R^5 = Me
(XXVIII) : R^5 = H

the phenyl than for the picolyl group to assume coplanarity with the propene system, and the former makes the greater contribution to the spectrum. The configurations of the isomers to which these spectra are referred are again confirmed by the order of elution and by cyclisation.

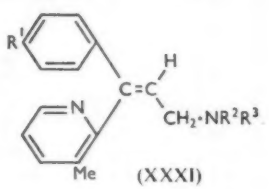
All the substituted alkenylamines described were prepared primarily for examination as antihistamines; many were found by Mr. A. F. Green of these Laboratories to show high activity, one of the most active [3] being (XXVI*c*) (" Actidil ").



(XXIX)



(XXX)



(XXXI)

Experimental

Ketones.—The following ketones, and those listed in Table 1, were prepared by the Mannich reaction as described in Part III: [4] p-*chloro*-α-*methyl*-β-*piperidinopropiophenone*, m. p. **36—37°** [from light petroleum (b. p. 40—60°)] (Found: C, 67·6; H, 7·5; N, 5·3; Cl, 13·2. $C_{15}H_{20}ONCl$ requires C, 67·8; H, 7·5; N, 5·3; Cl, 13·4%) [*hydrochloride*, m. p. 175—176° (from ethanol) (Found: C, 59·4; H, 7·0; N, 4·4; Cl, 22·7. $C_{15}H_{20}ONCl,HCl$ requires C, 59·6; H, 6·9; N, 4·6; Cl, 23·5%)]; α-*methyl*-β-*pyrrolidinopropiophenone hydrochloride*, m. p. 149—150° [from acetone–ethanol (3 : 1)] (Found: C, 65·6; H, 7·8; N, 5·4; Cl, 13·8. $C_{14}H_{19}ON,HCl$ requires C, 66·3; H, 7·9; N, 5·5; Cl, 14·0%); p-*chloro*-α-*methyl*-β-*pyrrolidinopropiophenone*, b. p. 152—156°/0·1 mm. (Found: C, 66·1; H, 7·0; N, 5·5; Cl, 13·9. $C_{14}H_{18}ONCl$ requires C, 66·7; H, 7·1; N, 5·6; Cl, 14·1%).

4-*Chloro*-α-*phenyl*-β-*pyrrolidinopropiophenone* was prepared from benzyl *p*-chlorophenyl ketone [5] by the method used by Mannich and Lammering [6] for α-phenyl-β-piperidinopropiophenone, and after crystallisation from light petroleum (b. p. 60—80°) had m. p. 97° (Found: C, 72·7; H, 6·0; N, 4·9; Cl, 11·4. $C_{19}H_{20}ONCl$ requires C, 72·7; H, 6·4; N, 4·5; Cl, 11·3%).

β-*Piperidinobutyrophenone* was prepared from crotonophenone [7] by the method used by Stobbe and Rosenburg [8] for β-phenyl-β-piperidinopropiophenone, and after crystallisation from light petroleum (b. p. 40—60°) had m. p. 38° (Found: N, 6·0. $C_{15}H_{21}ON$ requires N, 6·1%).

β-*Pyrrolidinobutyrophenone*, similarly prepared, had b. p. 126—130°/0·4 mm. (Found: N, 6·8. $C_{14}H_{19}ON$ requires N, 6·5%).

[3] Green, *Brit. J. Pharmacol.*, 1953, **8**, 171.
[4] Adamson and Billinghurst, *J.*, 1950, 1039.
[5] Jenkins, *J. Amer. Chem. Soc.*, 1934, **56**, 682.
[6] Mannich and Lammering, *Ber.*, 1922, **55**, 3510.
[7] Dufraisse and Demontoignier, *Bull. Soc. chim. France*, 1927, **41**, 843.
[8] Stobbe and Rosenburg, *J. prakt. Chem.*, 1912, **86**, 230.

p-*Chlorocrotonophenone*, prepared by the method used by Dufraisse and Demontoignier [7] for crotonophenone, had b. p. 160—164°/16 mm. (Found: C, 66·3; H, 4·6; Cl, 19·9. $C_{10}H_9OCl$ requires C, 66·6; H, 5·0; Cl, 19·7%). β-Piperidino-*p*-chlorobutyrophenone was prepared from it by Stobbe and Rosenburg's method,[8] but on attempted distillation it decomposed; it was therefore used for reaction with pyridyl-lithium (see below) without further purification.

2-*Pyridyl-alcohols*.—1-Phenyl-1-2′-pyridylethan-1-ol (XII*a*),[9] 1-*p*-chlorophenyl-1-2′-pyridylethan-1-ol (XII*b*),[3] 1-phenyl-1-2′-pyridylpropan-1-ol (XI*a*),[9] and the alcohols listed in Tables 2 and 3 were prepared from the corresponding ketones by reaction with 2-pyridyl-lithium as described in Part III.[4] The 2-3′-picolyl-alcohols (XXIX*a* and *b*) were similarly prepared, from 2-bromo-3-picoline.

Dehydration of the Alcohols to the Mixed Isomeric Alkenylamines.—The alcohols listed in Tables 2 and 3 were, with exceptions noted below, dehydrated to the mixed isomeric alkenylamines by heating them in sulphuric acid (85% v/v) (10 parts) at 100° for ½ hr. and working up as described previously.[4] The oxalates of the mixed alkenylamines, prepared in hot ethanol by addition of 1·1 mol. of anhydrous oxalic acid, usually crystallised on cooling but occasionally separated only on the addition of ether or ethyl acetate.

Separation of the Diasteroisomers of 1-p-*Chlorophenyl*-1-2′-*pyridyl*-3-*pyrrolidinobutan*-1-*ol* (XX*c*).—The crude alcohol (59 g.), which did not solidify, was converted into its oxalate with oxalic acid (22·5 g.) in a small volume of ethanol. After 12 hr. the solid oxalate (25 g.) was filtered off and washed with ethanol and ether, then was converted into the base, which solidified and after crystallisation from light petroleum (b. p. 60—80°) gave one *isomer* (9·0 g.) as prisms, m. p. 115—117°. The mother-liquors from the oxalate preparations were evaporated to dryness. The oxalate was converted into the base, which was distilled (25 g.; b. p. 170—200°/0·2 mm.). This solidified and after recrystallisation from a small volume of light petroleum (b. p. 40—60°) gave the second *isomer* (14 g.) as prisms, m. p. 105—106°, depressed to m. p. 80—85° on admixture with the first. Each isomer gave the same alkenylamine isomers on dehydration.

Separation of the Mixed Isomeric Alkenylamines (*Table* 4): cis- *and* trans-2-*Methyl*-1-*phenyl*-3-*piperidino*-1-2′-*pyridylprop*-1-*ene* (IIa) *and* (VII*a*).—(i) Fractional crystallisation of the mixed isomeric oxalates from ethanol gave the sparingly soluble trans-*oxalate* as colourless needles, m. p. 175—176°. The corresponding *base* had m. p. 85—86°. The oxalate recovered from the mother-liquors was converted into the base, which solidified and after several crystallisations from light petroleum (b. p. 40—60°) gave pure cis-*base* as prisms, m. p. 100—102°, depressed on admixture with *trans*-base to 75—79°. The cis-*oxalate* formed prisms, m. p. 125°. (ii) Mixed isomeric bases (3 g.) were submitted to ion-exchange chromatography as described in Part V.[1] The eluate was collected in fourteen fractions, all of which deposited crystalline material. Samples of solid were removed from every third fraction and dried on porous tile. The m. p.s and mixed m. p.s showed fractions 1—7 to contain pure *trans*-isomer, m. p. 83—85°, and fractions 10—14 to contain pure *cis*-isomer, m. p. 98—101°.

cis- *and* trans-1-p-*Chlorophenyl*-2-*methyl*-3-*piperdino*-1-2′-*pyridylprop*-1-*ene* (II*b*) *and* (VII*b*).—The sparingly soluble trans-*oxalate* crystallised from ethanol as rods, m. p. 201—202°. The oxalate recovered from the mother-liquors was converted into the base and submitted to ion-exchange chromatography, 42 fractions being collected. Although the ultraviolet absorption spectra of the two isomers determined photoelectrically were almost identical, the Holiday cam-plate [10] of the *trans*-isomer showed well-defined fine structure, a feature present in fractions 1—10 and absent in fractions 12—42. The latter were therefore collected and converted into cis-*oxalate*, plates (from ethanol–ether), m. p. 75—77° depressed to 68—71° on admixture with *trans*-oxalate.

cis- *and* trans-2-*Methyl*-1-*phenyl*-1-2′-*pyridyl*-3-*pyrrolidinoprop*-1-*ene* (II*c*) *and* (VII*c*).—The sparingly soluble trans-*oxalate* crystallised from ethanol as needles, m. p. 158—159°. The corresponding base had m. p. 55°. The oxalate recovered from the mother-liquors was converted into the base and submitted to base-exchange chromatography, twenty-two fractions being collected all of which deposited crystals. Fractions 1—6 contained *trans*-isomer, m. p. 52—54°. Fractions 12—22 had m. p.s in the range 65—70°, and were united and worked up to give pure cis-*base*, m. p. 69—70°, depressed on admixture with *trans*-isomer to 45—47°.

cis- *and* trans-1-p-*Chlorophenyl*-2-*methyl*-1-2′-*pyridyl*-3-*pyrrolidinoprop*-1-*ene* (II*d*) *and*

[9] Tilford, Shelton, and Van Campen, jun., *J. Amer. Chem. Soc.*, 1948, **70**, 4004.
[10] Holiday, *J. Sci. Instr.*, 1937, **14**, 166.

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(VII*d*).—The mixed isomeric oxalates were crystallised several times from ethanol, to give trans-*oxalate*, needles, m. p. 216°. The mother-liquors were evaporated, the residual oxalate was dissolved in boiling ethyl acetate and filtered from a little *trans*-oxalate, and the ethyl acetate filtrate evaporated to small volume. On cooling, crystals separated and after crystallisation from ethanol–ether gave cis-*oxalate*, m. p. 134—135°. The isomers were also separated by base-exchange chromatography as described above for the piperidino-analogue.

cis- *and* trans-1-p-*Chlorophenyl*-2-*phenyl*-1-2′-*pyridyl*-3-*pyrrolidinoprop*-1-*ene* (III*b*) *and* (VIII*b*).—(i) The alcohol (10 g.) was dehydrated by solution in 98% sulphuric acid (100 ml.) at room temperature for 3 hr. The mixed isomeric alkenylamines (9·2 g.) solidified. They were converted into the oxalates, which were separated by fractional crystallisation from ethanol and ethanol–ether into the less soluble trans-*oxalate*, m. p. 151—152°, and the more soluble cis-*oxalate*, m. p. 147—148°. The trans-*base* had m. p. 104—105° and the cis-*base* had m. p. 110°, depressed on admixture with *trans*-isomer to 82—88°. (ii) The mixed bases were separated by base-exchange chromatography into forty fractions, from each of which crystals separated. On the basis of the m. p.s and mixed m. p.s, fractions 5—22 were united and worked up to give *trans*-isomer, m. p. 44—45°, and fractions 26—40 similarly gave *cis*-base, m. p. 110°, depressed on admixture with the *trans*-isomer to 83—87°.

Isomeric 1 : 2-*Diphenyl*-3-*piperidino*-1-2′-*pyridylprop*-1-*ene* (III*a*) *and* (VIII*a*).—The alcohol (20 g.), similarly dehydrated, gave mixed alkenylamines (18 g.) which partly solidified. The solid portion (11 g.), filtered from the oil, recrystallised from light petroleum (b. p. 40—60°) to give an *isomer*, m. p. 91—92°. Separation of the mixed isomers by base-exchange chromatography gave the same solid isomer, m. p. 91—92°, in the head fractions, and oil in the tail fractions, whence no solid hydrochloride or oxalate was obtained.

cis-1 : 3-*Diphenyl*-3-*piperidino*-1-2′-*pyridylprop*-1-*ene* (X*a*).—The alcohol (10 g.), similarly dehydrated, gave alkenylamine (8·4 g.), which slowly solidified. This was separated by ion-exchange chromatography into 35 fractions, of similar spectrum ($\lambda_{max.}$ 250 mμ). The material crystallised from light petroleum, to give the cis-*base*, m. p. 77—79°. From alcohol dehydrated in 85% sulphuric acid at 100° for ½ hr. no water-insoluble product was recovered.

cis- *and* trans-1-(3-*Methyl*-2-*pyridyl*)-1-*phenyl*-3-*pyrrolidinoprop*-1-*ene* (XXX*a*) *and* (XXXI*a*).—The mixed oxalates were separated by fractional crystallisation from ethanol and ethanol–ether into the less soluble trans-*oxalate*, m. p. 158—160°, and the more soluble cis-*oxalate*, prisms, m. p. 152°.

cis- *and* trans-1-p-*Chlorophenyl*-1-(3-*methyl*-2-*pyridyl*)-3-*pyrrolidinoprop*-1-*ene* (XXX*b*) *and* (XXXI*b*).—(i) The isomeric oxalates were separated by fractional crystallisation from ethanol and ethanol–ether into the less soluble cis-*oxalate*, plates, m. p. 175—176°, and the more soluble trans-*oxalate*, m. p. 140—141°. (ii) Mixed bases were submitted to base-exchange chromatography. The spectra of the fractions were not sufficiently dissimilar to define the transition from *trans*- to *cis*-isomer. However, on an arbitrary basis the first third of the fractions was worked up to give pure *trans*-oxalate, m. p. 140°, and the last third of the fractions to give pure *cis*-oxalate, m. p. 175°.

cis- *and* trans-1-2′-*Pyridyl*-3-*pyrrolidino*-1-o-*tolylprop*-1-*ene* (XXV*a*) *and* (XXVII*a*).—The mixed isomeric bases were separated [11] by base-exchange chromatography, controlled spectroscopically, the ratio of the optical densities at 290 and 270 mμ being used (Figs. 2 and 3 of ref. 11 refer to the separation of this pair of isomers).

cis- *and* trans-1-(2 : 4-*Dimethylphenyl*)-1-2′-*pyridyl*-3-*pyrrolidinoprop*-1-*ene* (XXV*b*) *and* (XXVII*b*), *and* cis- *and* trans-1-(2 : 5-*Dimethylphenyl*)-1-2′-*pyridyl*-3-*pyrrolidinoprop*-1-*ene* (XXV*c*) *and* (XXVII*c*).—In each case the isomeric bases were separated by ion-exchange chromatography, controlled by the cam-plate method.[10]

The two examples lacking the tertiary amino-group [Table 4, (XIV) and (XV), *a* and *b*], the three γ-methyl-substituted examples [Table 4, (IV) and (IX), *a*, *b*, and *c*] and all the alkyl substituted examples in Table 5 not containing an *o*-methyl substituent were separated by base-exchange chromatography controlled by the ultraviolet absorption spectra of the fractions.

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Langley Court, Beckenham, Kent. [*Received, July 15th*, 1957.]

[11] Jones in "Ion Exchange and Its Applications" (Report on Symposium), Soc. Chem. Ind., London, 1955, p. 164.

62. *Aminoalkyl Tertiary Carbinols and Derived Products. Part VII.* A New Synthesis of 1-Arylpyrrocolines.*

By P. A. Barrett.

The 3-(tertiary amino)-1-aryl-1-2′-pyridylalkan-1-ols (I) and (XII) and the 3-(tertiary amino)-1-aryl-1-2′-pyridylalkenes (II) and (XIII) cyclise on treatment with boiling acetic anhydride to the corresponding 1-arylpyrrocolines (III), (V), and (XIV). Under comparable conditions the *cis*-isomers of the alkenes (II) and (XIII) give higher yields of pyrrocoline than the corresponding *trans*-isomers. Simultaneously with cyclisation, the alkanols and alkenes undergo alternative degradations analogous to those suffered by the corresponding diphenyl-alkanols and -alkenes on treatment with acetic anhydride.

In Part V [1] it was shown that *cis*-1-*p*-chlorophenyl-1-2′-pyridyl-3-pyrrolidinoprop-1-ene † (*cis*-II*b*) was cyclised by acetic anhydride, with loss of the pyrrolidino-group, to 3-acetyl-1-*p*-chlorophenylpyrrocoline (III*b*), under conditions which gave none from the *trans*-isomer (*trans*-II*b*).

As mentioned in Part VI,[2] it has now been found that by using different experimental conditions the yield of acetylpyrrocoline (III*b*) from the *cis*-alkenylamine (II*b*) is greatly increased, and under these conditions the same pyrrocoline is obtained, though in lower yield, from the *trans*-isomer. This cyclisation is general. The alkenylamines [1,2] (II*a*—*i*) all gave pyrrocolines (III) or (V), and where both configurations have been examined a higher yield was obtained from the *cis*- than from the *trans*-isomers. From any alkenylamine (II) in which R^3 is methyl or phenyl, the product of cyclisation is the corresponding 3-methyl- or 3-phenyl-pyrrocoline (V*g*, *h*, and *i*). Thus, the alkenylamine (II*h*) on cyclisation gave 1-*p*-chlorophenyl-3-methylpyrrocoline (V*h*), whose constitution was confirmed by its identity with a sample prepared by the Scholtz–Chichibabin reaction [3,4] from 2-4′-chlorobenzylpyridine and propionic anhydride. From any alkenylamine (II) in which R^3 is hydrogen, the product of cyclisation is the corresponding 3-acetylpyrrocoline (III), formed by the acetylation, by the excess acetic anhydride always present, of the reactive 3-position of the pyrrocoline (V; $R^3 = H$), for the presence of which, as an intermediate in the reaction, evidence is adduced below. The invariable survival of the alkenylamine substituents R^2 and R^3, when these are methyl or phenyl, in the resultant pyrrocoline proves that it is the carbon atoms of the alkenylamine chain which compose the five-membered ring of the pyrrocoline, and that the latter is not derived from a molecule of acetic anhydride by reaction with a breakdown fragment of alkenylamine by a Scholtz–Chichibabin [3,4] type of reaction.

It has further been shown that the alcohols (I) also cyclise to the corresponding pyrrocolines on treatment with acetic anhydride, and evidence will be presented to show that the cyclisation of the alcohols (I) does not proceed through the alkenylamines (II).

The present paper deals with these reactions as new preparative routes to substituted pyrrocolines. The results as they are relevant to the stereochemistry of the alkenylamine isomers *cis*-(II) and *trans*-(II), were discussed in Part VI. The constitution of 3-acetyl-1-*p*-chlorophenylpyrrocoline (III*b*) was rigorously established earlier,[1] and that of 1-*p*-chlorophenyl-3-methylpyrrocoline (V*h*) is established above. The constitution of the other pyrrocolines is confirmed by their similar, highly characteristic ultraviolet absorption.

Reaction of the Alcohols (I) *with Acetic Anhydride.*—This reaction is complex and

* Part VI, preceding paper.

† As in earlier papers, *cis* and *trans* refer to the relation of the pyridyl and the aminoalkyl group.

[1] Adamson, Barrett, Billinghurst, and Jones, *J.*, 1957, 2315.

[2] *Idem*, preceding paper.

[3] Chichibabin and Stepanow, *Ber.*, 1929, **62**, 1068.

[4] Scholtz, *Ber.*, 1912, **45**, 734.

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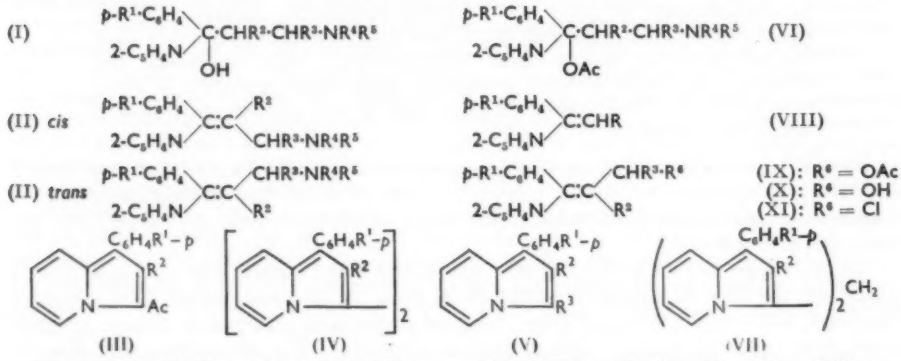
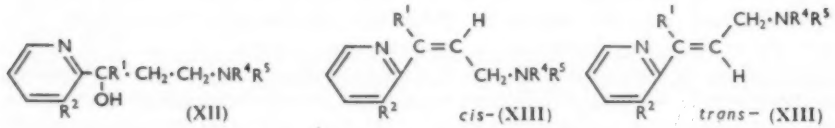
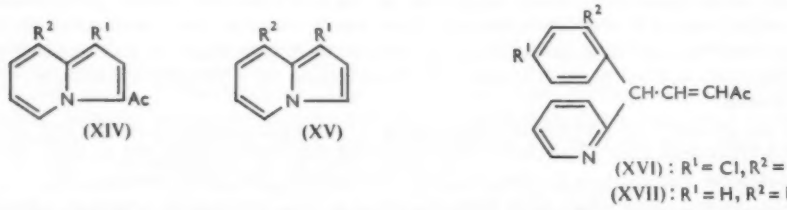
follows at least two paths. The alcohol (I*b*) is rapidly esterified to (VI*b*), which is intermediate in the rather slow reactions which occur on further boiling. After 3 hours' boiling some acetate (VI*b*) was recovered, but after 16 hours reaction was complete. In addition to the pyrrocoline (III*b*), there were isolated the dipyrrocolylmethane derivative (VII*b*) and the *p*-chlorophenylpyridylethylene (VIII*b*). It is apparent that the alcohol undergoes simultaneously both (i) ring closure to the pyrrocoline (V*b*), most of which is rapidly acetylated to (III*b*), and (ii) a degradation involving cleavage of the carbon chain similar



Compounds I—IX	R^1	R^2	R^3	R^4R^5
a	H	H	H	$<[CH_2]_4$
b	Cl	H	H	,,
c	H	Me	H	$<[CH_2]_5$
d	Cl	Me	H	,,
e	H	Ph	H	,,
f	Cl	Ph	H	$<[CH_2]_5$
g	H	H	Me	,,
h	Cl	H	Me	$<[CH_2]_4$
i	H	H	Ph	$<[CH_2]_5$





Compounds XII—XV	R^1	R^2	R^4R^5
a	*p*-MeO·C_6H_4	H	$<[CH_2]_4$
b	*p*-C_6H_4Me	H	,,
c	*o*-C_6H_4Me	H	,,
d	Ph	Me	,,
e	*p*-C_6H_4Cl	Me	$<[CH_2]_4$
f	5-Chloro-2-thienyl	H	,,
g	2-Pyridyl	H	Me_2

to that shown by Adamson [5] to occur with analogous diphenylpropanols. Degradation of the alcohol (I*b*) by the second route leads to *p*-chlorophenylpyridylethylene (VIII*b*), acetylpyrrolidine, and formaldehyde. The dipyrrocolylmethane (VII*b*) is clearly formed by condensation of the formaldehyde (produced by this second reaction) with pyrrocoline (V*b*) (simultaneously under production by the ring closure). Analogous products have

[5] Adamson, *Nature*, 1949, **164**, 500.

been isolated from several of the other examples examined. The reaction pattern is thus general, though the proportion of alcohol reacting by one or the other route varies considerably in examples containing different groups R^1, R^2, and R^3. Thus, the alcohol (I*i*) gave 60% of the pyrrocoline (V*i*) whereas the alcohol (I*g*) gave only 5% of the pyrrocoline (V*g*) and 60% of the phenylpyridylethylene (VIII*g*). The evidence available suggests that within the limited range ($NR^4R^5 = N < [CH_2]_4$, $N < [CH_2]_5$, or NMe_2) the nature of the amino-group used in conjunction with any given substituents R^1, R^2, and R^3 does not affect the course of the reaction. The course of the reaction was not markedly affected by addition of acetic acid or sodium acetate.

Reaction of the Alkenylamines (II) *with Acetic Anhydride.*—The yield of pyrrocoline (III) or (V) from the alkenylamines (II) is however very dependent on the experimental conditions. Ring closure by the method described in Part V gave *ca.* 10% of the pyrrocoline (III*b*) from the *cis*-allylamine (II*b*), and no isolable pyrrocoline from the *trans*-isomer. By the addition of acetic acid and anhydrous sodium acetate to the acetic anhydride, and employing slow addition (1½—2 hours) of the *cis*-allylamine (II*b*) to the reaction mixture the yield of (III*b*) was raised to *ca.* 50% and the production of tar substantially reduced. Under these conditions the *trans*-isomer (II*b*) gave (III*b*), but in consistently lower yield (*ca.* 25%). These preferred conditions were used for all subsequent examples. The yields of pyrrocoline obtained from the *cis*-alkenylamines in different examples were in the range of 25—50%.

As with the alcohols, the reaction of the alkenylamines (II) with acetic anhydride is complex, and a variety of products in addition to the pyrrocolines (III) or (V) has been isolated. Some of them occur only in isolated examples and are discussed below. A more general phenomenon is the formation of the acetoxy-compounds (IX). From all those alkenylamines where it has been sought (II*a*—*g*, *i*), evidence of their production was found. They are end-products, unchanged on further treatment with acetic anhydride. The esters (IX*c*, *e*, *f*) were isolated as crystalline solids; (IX*b*, *d*) were characterised by hydrolysis to the corresponding solid alkenols (X*b*, *d*). [The acetoxy-compound (IX*d*) was hydrolysed to the alkenol (X*d*) by boiling aqueous-alcoholic potassium hydroxide. Boiling concentrated hydrochloric acid converted the ester into the corresponding chloro-compound (XI*d*).] In the products of some cyclisations the acetoxy-compounds (IX) were accompanied by the corresponding alkenols (X*b*, *d*, *e*, *f*), the latter probably derived from the former during working up, since the acetoxy-compounds (IX) are very rapidly hydrolysed by 2N-hydrochloric acid. In four examples (II*b*, *c*, *d*, *e*) in which the acetoxy-compound was isolated from both separated isomers of the alkenylamine, that from the *trans*-isomer was identical with, and was obtained in higher yield than, that from the *cis*-isomer. Three of these examples were of the 2-substituted type (II; R^2 = Me or Ph) for which the absorption spectra are not diagnostic [2] of the stereochemical configuration, but in the fourth the absorption spectra showed that the single acetoxy-compound (IX*b*) formed both from *cis*- and *trans*-alkenylamines (II*b*), has the *trans*-configuration, and on hydrolysis gave the *trans*-alkenol (X*b*). It appears probable that all acetoxy-compounds (IX) and alkenols (X) isolated from the reactions have the *trans*-configuration.

The formation of both pyrrocoline (III) and *trans*-acetoxy-compound (IX) from both isomers, a higher proportion of the former from the *cis*-alkenylamine and of the latter from the *trans*-alkenylamine, is interpreted in terms of a fundamentally sharp distinction between the reactions undergone by the two forms, the *cis*-compound giving only pyrrocoline and the *trans*-isomer only *trans*-acetoxy-compound, confused by a slow isomerisation of each isomer to the other during the reaction. This sharp distinction has been realised in some pairs of alcohols, to be described in Part VIII, geometrically isomeric with respect to a *cyclo*alkane ring, in which the possibility of isomerisation is excluded.

Adamson [5] showed that 3-(tertiary amino)-1 : 1-diphenylprop-1-enes, when boiled with acetic anhydride, gave high yields of acetoxy-compounds analogous to those (IX) of the present series. The alcohols (I) and the alkenylamines (II) thus react with acetic

TABLE 1. *1-Substituted 3-acetylpyrrocolines* (III) *and* (XIV) (*italicised wavelengths indicate inflections*).

Compound	R¹	R²	M. p.	Absorption max. in EtOH: λ (mμ)						10⁻³ε					
IIIa	H	H	82—83°	235	*248*	267	*285*	370	—	14	14·8	30	17·5	15	—
IIIb	Cl	H	173—174	220	—	265	285	369	—	18	—	26	18	15	—
IIIc	H	CH_3	127—128	225	*258*	274	—	355	373	13	16	23	—	8·9	12
IIId	Cl	CH_3	154	225	245	273	—	363	377	21·2	15·2	25·5	—	14·5	12·2
IIIe	H	Ph	175—176	—	*247*	270	—	373	—	—	20	25	—	13	—
IIIf	Cl	Ph	181—182	*225*	—	267	—	371	—	20	—	24	—	12·5	—
XIVa	*p*-MeO·C_6H_4	H	122	239	—	272	—	366	—	18·5	—	34·5	—	13·7	—
XIVb	*p*-C_6H_4Me	H	133	*236*	—	269	—	373	—	14·5	—	30·5	—	14	—
XIVc	*o*-C_6H_4Me	H	65	*220*	—	266	—	367	*385*	12	—	20·5	—	9·6	7·5
XIVd	Ph	Me	100—101	224	*250*	270	—	365	—	14·5	13·9	24·2	—	14·5	—
XIVe	*p*-C_6H_4Cl	Me	112—113	223	—	264	—	370	—	22	—	28	—	15·2	—
XIVf	[a]	H	119	226	—	265	308	361	—	20	—	17·9	14·3	14·7	—
XIVg	2-Pyridyl	H	112	—	*248*	263	309	360 [b]	—	—	14·9	22·1	14·9	16·8	—

[a] Broad band. [b] 5-Chloro-2-thienyl.

Compound	Formula	Found (%): C	H	N	Cl	Required (%): C	H	N	Cl
IIIa	$C_{16}H_{13}ON$	81·1	5·3	6·0	—	81·7	5·6	6·0	—
IIIb	$C_{16}H_{12}ONCl$	71·4	4·8	4·9	13·0	71·2	4·5	5·2	13·2
IIIc	$C_{17}H_{15}ON$	81·6	6·0	5·6	—	81·9	6·0	5·6	—
IIId	$C_{17}H_{14}ONCl$	72·2	5·2	5·1	12·1	71·9	4·9	4·9	12·5
IIIe	$C_{22}H_{17}ON$	84·9	5·5	4·8	—	84·9	5·5	4·5	—
IIIf	$C_{22}H_{16}ONCl$	76·6	4·3	4·0	10·3	76·5	4·6	4·1	10·3
XIVa	$C_{17}H_{15}O_2N$	76·9	5·6	5·2	—	77·0	5·7	5·3	—
XIVb	$C_{17}H_{15}ON$	82·0	6·0	5·5	—	81·9	6·0	5·6	—
XIVc	$C_{17}H_{15}ON$	82·4	6·2	6·1	—	81·9	6·0	5·6	—
XIVd	$C_{17}H_{15}ON$	81·8	5·6	6·1	—	81·9	6·0	5·6	—
XIVe	$C_{17}H_{14}ONCl$	72·1	5·0	5·0	12·5	71·9	4·9	4·9	12·5
XIVf	$C_{14}H_{10}ONClS$	61·0	3·5	11·5 [c]	13·2	61·0	3·6	11·6 [c]	12·9
XIVg	$C_{15}H_{12}ON_2$	76·3	5·3	11·7	—	76·3	5·1	11·9	—

[c] Sulphur analysis.

TABLE 2. *1-Substituted pyrrocolines* (V) *and* (XV).

Compound	R¹	R²	R³	M. p. (b.p./mm.)	Absorption max. in EtOH: λ (mμ)						10⁻³ε					
Va	H	H	H	67—68° [a]	236	—	*283*	305	—	362	23	—	8·6	12	—	3·4
Vb	Cl	H	H	73 [a]	239	—	—	313	—	360	32	—	—	15	—	6
Vc	H	Me	H	140—145/0·5	242	—	284	310	—	347	24	—	7·4	7·8	—	2·9
Vd	Cl	Me	H	77 [a,b]	242	—	*285*	315	—	360	25	—	6·8	11	—	4·5
Ve	H	Ph	H	112 [a]	250	264	—	305	—	360	32	24·5	—	9·2	—	5·6
Vf	Cl	Ph	H	118 [b]	248	273	—	307	—	357	38	25	—	11·6	—	5·1
Vg	H	H	Me	67—68 [a]	239	—	*280*	312	*355*	373	32	—	6	12	4·1	4·5
Vh	Cl	H	Me	91—92 [a]	243	—	277	320	—	385	20	—	4·9	13	—	4·8
Vi	H	H	Ph	115—116 [b]	238	—	274	309	*345*	*336*	28	—	20	19·5	10	4
XVa	[d]	H	—	72—73 [a,c]	240	—	277	305	—	367	25·6	—	10·5	12·4	—	4·25
XVd	Ph	Me	—	155—160/0·5	235	—	—	303	—	350	28	—	—	8·3	—	3·8

[a] From light petroleum (b. p. 40—60°). [b] From ethanol. [c] From light petroleum (b. p. 60—80°). [d] *p*-MeO·C_6H_4.

TABLE 2. (*Continued.*)

Compound	Formula	Found (%) C	H	N	Cl	Required (%) C	H	N	Cl
V*a*	$C_{14}H_{11}N$	87·1	5·6	7·4	—	87·0	5·7	7·3	—
V*b*	$C_{14}H_{10}NCl$	73·9	4·5	6·1	15·3	73·8	4·4	6·2	15·6
V*c*	$C_{15}H_{13}N$ [d]	87·1	6·3	—	—	86·9	6·3	6·8	—
V*d*	$C_{15}H_{12}NCl$	74·7	5·3	6·1	14·2	74·6	5·0	5·8	14·7
V*e*	$C_{20}H_{15}N$	89·2	5·7	5·5	—	89·2	5·6	5·2	—
V*f*	$C_{20}H_{14}NCl$	78·7	4·9	4·7	11·6	79·1	4·6	4·6	11·7
V*g*	$C_{15}H_{13}N$	87·0	6·4	6·5	—	86·9	6·3	6·8	—
V*h*	$C_{15}H_{12}NCl$	74·6	4·9	5·9	14·3	74·6	5·0	5·8	14·7
V*i*	$C_{20}H_{15}N$	89·7	5·7	5·2	—	89·2	5·6	5·2	—
XV*a*	$C_{15}H_{13}ON$	80·7	5·8	6·5	—	80·7	5·9	6·3	—
XV*d*	$C_{15}H_{12}N$	87·0	6·4	7·0	—	86·9	6·3	6·8	—

[d] Chichibabin, *Ber.*, 1927, **60**, 1607.

anhydride in different ways, the ring closure to pyrrocoline, necessarily confined to compounds containing a pyridyl group, occurring simultaneously with more general methods of decomposition characteristic of the corresponding diphenyl-propanols and -alkenylamines. As no *trans*-acetoxy-compound (IX) could be found among the products from the alcohols (I) and acetic anhydride, it is concluded that this reaction does not involve initial dehydration to the alkenylamines (II).

Some Extensions of the Reaction.—A number of pyrrocolines have been prepared which extend the scope of the reaction described above. Three examples (XIV*a*, *b*, and *c*) containing substituted phenyl groups were prepared from the alcohols (XII) and the corresponding alkenylamines (XIII). Two 8-methylpyrrocolines (XIV*d* and *e*) were prepared from the picolylalkenylamines (XIII*d* and *e*). Pyrrocolines (XIV*c* and *e*) were prepared from each of the pure isomeric alkenylamines, the difference between the *cis*- and the *trans*-isomers being sharper than in earlier examples: the *cis*-isomers gave high yields of pyrrocoline, the *trans*-isomers gave none. It may be significant that both structures contain [2] highly hindering methyl groups. Two examples of pyrrocolines carrying heterocyclic substituents in the 1-position have also been prepared, (XIV*f*) from the alkenylamine, and (XIV*g*) from the alcohol (the corresponding alkenylamine is unknown). Earlier attempts [6] to dehydrate dipyridyl-alcohols were unsuccessful.

Other By-products of the Alkenylamine Cyclisations.—The acetylpyrrocolines (III*a* and *b*, and XIV*a*) were accompanied by smaller amounts of compounds which on the basis of analysis and ultraviolet spectra are believed to be the dipyrrocolyl compounds (IV*a*; IV*b*; and IV, R^1 = OMe, R^2 = H). The ultraviolet spectra show maxima corresponding in wavelength to those of the 1-arylpyrrocolines (V*a*; V*b*; and XV*a*) but with increased intensity. The dipyrrocolyls (IV*a* and *b*) have also been obtained from the hydrobromides of the alkenylamines (II*a* and *b*) by reaction with hot quinoline. The elements of acetic anhydride do not therefore participate in their formation. Their formulation as dipyrrocolyls appears certain, and it is more probable on mechanistic grounds that union should be in the 3- than in the 2-position.

Accompanying the 3-acetyl-1-*o*-tolylpyrrocoline (XIV*c*) in the cyclisation of the *cis*-alkenylamine (XIII*c*), and constituting the sole product from the *trans*-isomer, was a colourless basic compound (Q). An analogous compound (P) accompanied the acetoxy-compound (IX*b*) in the product of cyclisation of the *trans*-alkenylamine (II*b*), and was separated from it by base-exchange chromatography controlled by the absorption spectra of the fractions. Analysis suggested that both compounds were isomeric with the corresponding acetylpyrrocolines. In each, the single oxygen atom was not determinable as acetyl, and microreduction showed the presence of a double bond. The ultraviolet absorption spectra of compounds (P) and (Q) were almost identical and highly characteristic, each showing double peaks at 258 and 266 mμ (ε 4600), and at 320 and 330 mμ (ε *ca.* 300).

[6] Adamson and Billinghurst, *J.*, 1950, 1039.

The former peak so closely resembles the absorption of the corresponding alcohols, *e.g.*, (I*b*), and alkanes, as to exclude both the presence of αβ-unsaturation and the possibility that the compounds might be the appropriately substituted 1- or 3-2′-pyridylindenes. 3-2′-Pyridylindene has been prepared and shows a spectrum very similar to 2-vinylpyridine.[1] Indene shows [7] absorption closely resembling that of styrene, and 1-2′-pyridylindene would be unlikely to absorb less strongly. Chromic acid oxidation of compound (P) gave a compound which is probably α-*p*-chlorophenyl-α-2-pyridylacetic acid. Taken in conjunction with the spectral evidence, this supports the formulation of compounds (P) and (Q) as the substituted 1-phenyl-1-2′-pyridylpent-2-en-4-ones (XVI) and (XVII), though the analytical figures agree better with empirical formulæ containing two hydrogen atoms less, and final proof of structure is lacking. The ultraviolet absorption at 320—330 mμ is not only too intense to be referred to the crotonyl ketone chromophore, but the intensity is unaffected (though there is some alteration in $\lambda_{max.}$) on reduction of the ethylenic bond. My colleague, Dr. A. J. Everett, suggests that since the carbonyl frequency is normal (at 1700 cm.$^{-1}$) an interaction between the carbonyl-carbon atom and the pyridyl-nitrogen atom is responsible for the 320—330 mμ absorption.

From the ring closure of the γ-phenylalkenylamine (II*i*) there was isolated, in addition to 1 : 3-diphenylpyrrocoline (V*i*), a colourless, basic, unidentified isomer of the alkenylamine (II*i*). Its ultraviolet absorption spectrum was almost the same as that of the parent alcohol (I*i*). It does not, therefore retain the αβ-double bond of the alkenylamine (II*i*).

Hydrolysis of the Acetylpyrrocolines.—In many cases the 3-acetylpyrrocolines (III) and (XIV) have been hydrolysed to the parent pyrrocolines (V) and (XV) (Table 2), generally in high yield, by 5—10 minutes' boiling with concentrated hydrochloric acid. In a few cases (*e.g.*, III*b*) long boiling (1 hr.) was necessary to dissolve the sparingly soluble acetylpyrrocoline hydrochloride. The ultraviolet spectra of all the acetylpyrrocolines (III) and (XIV) (Table 1) are broadly similar, and differ sharply from those of the non-acetylated pyrrocolines (V) and (XV) (Table 2) which are again closely related. In both groups the similarity of the spectra confirms the constitutions.

Experimental

Italicised wavelengths represent inflections.

3-*Acetyl*-1-p-*Chlorophenylpyrrocoline* (III*b*).—(a) *From the alcohol.* (i) The alcohol [6] (I*b*) (30 g.) and acetic anhydride (300 ml.) were boiled under reflux for 3 hr. Excess of anhydride was removed *in vacuo* and the residue treated with water (1 l.). The sticky solid (A) was filtered off and washed with water. The filtrate was basified with ammonia. The oil was isolated with ether, and solidified (13 g.). Recrystallisation from light petroleum (b. p. 40—60°) gave 1-p-*chlorophenyl*-1-2′-*pyridyl*-3-*pyrrolidinoprop*-1-*yl acetate* (VI*b*), m. p. 82—83° (Found: C, 66·8; H, 6·4; N, 7·7; Cl, 9·9; Ac, 12·2. $C_{20}H_{23}O_2N_2Cl$ requires C, 66·9; H, 6·4; N, 7·8; Cl, 9·9; Ac, 12·0%), $\lambda_{max.}$ 225, 255, and 262 mμ (ε 12,800, 3900, 4200 in EtOH). The material (A) was washed with ether, which removed dark oil and left friable solid (B). The ether filtrate was extracted twice with 2N-hydrochloric acid. The aqueous layer was basified with ammonia, and the oil (2·0 g.) isolated with ether and converted into hydrochloride (by ethereal hydrogen chloride) which solidified when seeded and on crystallisation from a small volume of ethanol gave 1-*p*-chlorophenyl-1-2′-pyridylethylene hydrochloride (VIII*b*) (0·5 g.), m. p. 195—197°, unchanged on admixture with an authentic specimen [2] (Found: C, 62·2; H, 4·2; N, 5·4; Cl, 27·8. Calc. for $C_{13}H_{11}NCl_2$: C, 61·9; H, 4·4; N, 5·6; Cl, 28·2%). The solid (B) was boiled with ethanol [420 ml.; sufficient to dissolve the material had it all been (III*b*)] and filtered from undissolved solid (C). The filtrate deposited 3-acetyl-1-*p*-chlorophenylpyrrocoline [1] (III*b*) (4·7 g.), m. p. 173—174°. The solid (C) (1·7 g.), on recrystallisation from pyridine, gave *di*-(1-p-*chlorophenyl*-3-*pyrrocolyl*)*methane* (VII*b*) as straw-coloured needles, m. p. 255°,

[7] Morton and de Gouveia, *J.*, 1934, 911.

unchanged on admixture with an authentic specimen from 1-*p*-chlorophenylpyrrocoline (V*b*) and formaldehyde prepared earlier by my colleague, Dr. N. Whittaker (Found: C, 74·2; H, 3·9; N, 6·0; Cl, 15·1. $C_{29}H_{20}N_2Cl_2$ requires C, 74·5; H, 4·3; N, 6·0; Cl, 15·2%).

(ii) The alcohol (20 g.) and acetic anhydride (400 ml.) were boiled for 16 hr. and worked up as in (i). The aqueous layer gave, on basification, only 1·0 g. of brown oil which did not solidify on being seeded with the acetate (VI*b*). The ether-insoluble solid, on crystallisation, gave acetylpyrrocoline (III*b*) (9·1 g., 50%) and dipyrrocolylmethane (VII*b*) (0·9 g.).

(iii) The alcohol (5 g.) and acetic anhydride (25 ml.) were heated till just boiling and excess of anhydride immediately removed *in vacuo*. Working up as in (i) gave the acetate (VI*b*) (4·2 g.), m. p. and mixed m. p. 82—83°.

(b) *From the alkenylamine.* The alkenylamine (II*b*) used in the following experiments (i)—(vi) was prepared by dehydration of the alcohol (I*b*) in concentrated sulphuric acid at 0—10° for 2 hr. Such material has been shown [1] to be predominantly *cis*-isomer.

(i) Acetic anhydride (250 ml.), acetic acid (150 ml.), and sodium acetate (freshly fused and ground; 250 g.) were boiled under reflux (oil-bath), alkenylamine (II*b*) (25 g.) in acetic acid (100 ml.) was added during 1½ hr., and the mixture boiled for a further 1½ hr. The solvent was removed *in vacuo* and the residue treated with water (2 l.). After being kept overnight, the sticky black solid was filtered off and washed with water, then ether (60 ml. in portions) which removed much dark oil and left friable greyish-yellow material (14·8 g.). One crystallisation from ethanol (900 ml.) [with filtration from material (A)] gave acetylpyrrocoline (III*b*), pale yellow needles (12·0 g., 53%), m. p. 173—174°, raised on further crystallisation to 175—176°. Two similar experiments gave yields of 52% and 54%. The insoluble material (A) (0·9 g.) was crystallised from pyridine, to give *di*-(1-p-*chlorophenyl*-3-*pyrrocolyl*), deep yellow needles, m. p. 288—290° (Found: C, 74·2; H, 3·9; N, 6·3; Cl, 15·7. $C_{28}H_{18}N_2Cl_2$ requires C, 74·1; H, 4·0; N, 6·2; Cl, 15·7%), $\lambda_{max.}$ 238, 315, and 375 mμ (ε 35,000, 36,500, and 10,000 in dioxan).

(ii) Omitting the sodium acetate, (iii) reducing or (iv) omitting the acetic acid and (v) adding the alkenylamine all at once, reduced the yields of acetylpyrrocoline to (ii) 35%, (iii) 44%, (iv) 33%, and (v) 45%.

(vi) Isolation of by-products. Alkenylamine (II*b*) (100 g.) was cyclised as described under (i). After the addition of water (2 l.) the sticky solid (A) was filtered off and washed with water. The aqueous layer was basified with ammonia and extracted with ether, to give oil (B) (9·0 g.). The solid (A) was washed with ether (180 ml. in portions), and on crystallisation from ethanol gave acetylpyrrocoline (III*b*) (47·8 g.: m. p. 170—172°). The ether washings gave black oil (31 g.) which was extracted with boiling light petroleum (b. p. 60—80°) (3 × 400 ml.) with filtration from tar. The combined light petroleum extracts on evaporation gave a light brown oil (24 g.). This was dissolved in ether and extracted with successive 100 ml. portions of 2N-hydrochloric acid. The aqueous acid extracts were combined and basified with ammonia, and the oil isolated with ether, combined with (B), and distilled, to give a colourless oil (15·9 g.), b. p. 185—190°/0·2 mm. This oil (8·2 g.) was separated by ion-exchange chromatography, controlled by the ratio of the optical densities at 265 mμ and 282 mμ (referred to below as O.D.R.). The material eluted first, having O.D.R. 10, gave on distillation a *compound* (P) (2·1 g.) as a viscous, amber oil, b. p. 175—180°/0·1 mm. (Found: C, 71·3; H, 4·2; N, 5·2; Cl, 12·6; Ac, 1·4%; microreduction, 1·04 double bonds, calculated on *M* 270. $C_{16}H_{12}ONCl$ requires C, 71·3; H, 4·5; N, 5·2; Cl, 13·2%), $\lambda_{max.}$ 223, 257, 263, 315, and 320 mμ (ε 17,600, 4600, 4650, 300, and 260 in EtOH) [cf. the acetate (VI*b*) above]. The material eluted next (O.D.R. 1) was distilled, to give an oil (2·4 g.), b. p. 200—205°/0·1 mm. (Found: Ac, 11·3. $C_{16}H_{14}O_2NCl$ requires Ac, 15·0%), presumed from the acetyl determination to contain a substantial proportion of the acetoxy-compound (IX*b*), probably associated with some propenol (X*b*) (see below). It was hydrolysed for 2 hr. with 2N-hydrochloric acid (50 ml.) at 100°. Basification gave an oil which solidified and was filtered off, washed, dried, and recrystallised from ethanol and then from light petroleum (b. p. 80—100°), to give trans-3-p-*chlorophenyl*-3-2′-*pyridylprop*-2-*en*-1-*ol* (X*b*) as colourless plates (1·8 g.), m. p. 98° (Found: C, 68·8; H, 5·0; N, 5·9; Cl, 14·5. $C_{14}H_{12}ONCl$ requires C, 68·4; H, 4·9; N, 5·7; Cl, 14·5%), $\lambda_{max.}$ 235 and 277 mμ (ε 17,000 and 6500 in EtOH).

In a cyclisation of alkenylamine (II*b*) (400 g.) worked up similarly, the fraction having O.D.R. 1 deposited crystals when kept for several days. These were filtered off and crystallised to give propenol (X*b*) (6·6 g.), m. p. and mixed m. p. 97—98°.

(vii) Pure *trans*-1-*p*-chlorophenyl-1-2′-pyridyl-3-pyrrolidinoprop-1-ene [1] (II*b*) (44 g.) was treated as in (vi), giving acetylpyrrocoline (III*b*) (10·4 g., 26%), and a basic oil, b. p.

XUM

175—180°/0·1 mm. (17·1 g.), 10 g. of which were separated by ion-exchange chromatography into compound (P) (2·5 g.), having O.D.R. 10 (Found: C, 71·0; H, 4·5%), and the *acetoxy-compound* (IX*b*) (3·0 g.) having O.D.R. 1 (Found: Ac, 14·8. $C_{16}H_{14}O_2NCl$ requires Ac, 15·0%), $\lambda_{max.}$ 232 and 272 mμ (ε 18,500 and 6500 in EtOH). This material did not solidify but was hydrolysed, as described in (vi), to propenol (X*b*) (2·1 g.), m. p. 97—98°, not depressed on admixture with the sample described under (viii).

(viii) Pure *cis*-1-*p*-chlorophenyl-1-2′-pyridyl-3-pyrrolidinoprop-1-ene (II*b*) (freed from *trans*-isomer by ion-exchange chromatography as described in Part V [1]) (70 g.) was cyclised and worked up as in (vi), to give acetylpyrrocoline (III*b*) (38·5 g., 61%), m. p. 171—172°, and a basic oil (9·8 g.), b. p. 185—190°/0·2 mm. From the latter by ion-exchange chromatography no material having an O.D.R. of 10 was isolated. The material having O.D.R. 1, after working up and hydrolysis as described in (vi), gave the propenol (X*b*) (1·2 g.), m. p. 97—98°, not depressed on admixture with the sample described under (vii).

Oxidation of Compound (*P*).—The compound (2·0 g.), dissolved in acetic acid (60 ml.), was heated on the steam-bath for 10 min. with chromium trioxide (24 g.) in water (18 ml.) and acetic acid (100 ml.). The mixture was cooled, poured on ice, basified by aqueous sodium hydroxide, and extracted with ether. The aqueous layer was just acidified with hydrochloric acid (litmus). Extraction with ether gave oil which, after addition of a little water to dissolve acetic acid, deposited gum (0·8 g.) which, separated by decantation, crystallised from water to give α-*p*-*chlorophenyl*-α-2-*pyridylacetic acid*, colourless needles (0·5 g.), m. p. 116—117° (Found: C, 63·5; H, 4·3; N, 5·3; Cl, 13·6. $C_{13}H_{10}O_2NCl$ requires C, 63·0; H, 4·0; N, 5·7; Cl, 14·3%).

3-*Acetyl*-1-*phenylpyrrocoline* (III*a*).—(i) *From the alcohol.* 1-Phenyl-1-2′-pyridyl-3-pyrrolidinopropan-1-ol [6] (I*a*) (8 g.) and acetic anhydride (100 ml.) were boiled for 6 hr. After removal of excess of anhydride and addition of water, the separated oil was taken into ether, and the ether solution was washed with 2N-hydrochloric acid and evaporated to give a brown oil (2 g.), which solidified. Distillation gave a yellow oil, which after crystallisation from light petroleum (b. p. 60—80°) gave acetylpyrrocoline (III*a*) (1·2 g.), m. p. 81—82°, not depressed on admixture with the sample described under (iii).

(ii) 3-Dimethylamino-1-phenyl-1-2′-pyridylpropan-1-ol [6] [as (I*a*) but with $NR^4R^5 = NMe_2$] (5 g.), similarly treated, gave (III*a*) (0·5 g.), m. p. 82—83°.

(iii) *From the alkenylamine.* Alcohol (I*a*) (36 g.) was dehydrated by dissolution in 400 ml. of 85% sulphuric acid at 0° and storage for 4 hr. 1-Phenyl-1-2′-pyridyl-3-pyrrolidinoprop-1-ene (33 g.) was cyclised as described above. Addition of water gave a dark oil, which was extracted with ether. The aqueous layer was basified and the oil (A) isolated with ether. This ether extract was filtered (charcoal) and extracted with 2N-hydrochloric acid (5 × 200 ml.). The combined acid extracts were united and basified, and the oil was collected in ether, united with (A) (total, 10·2 g.), and distilled (b. p. 159—162°/0·2 mm.), to give a colourless mobile oil (7·5 g.) [Found: Ac, 11·8. Calc. for $C_{16}H_{15}O_2N$ (IX*a*): Ac, 17·0%]. This material was presumed to be a mixture, substantially acetoxy-compound (IX*a*), but containing probably propenol (X*a*) and/or the analogue of compound (P). The ether layer was evaporated to a brown oil (20 g.), which rapidly solidified. Distillation (b. p. 194—200°/0·2 mm.) gave 17 g. of a yellow oil which solidified and recrystallised from light petroleum (b. p. 60—80°), to give 3-*acetyl*-1-*phenyl-pyrrocoline* (III*a*) (14 g.), yellow prisms, m. p. 82—83°. The residue in the distillation flask solidified on addition of a few drops of light petroleum. It was lixiviated with a little chloroform, filtered, and recrystallised from light petroleum (b. p. 60—80°) to give *di*-(1-*phenyl*-3-*pyrrocolyl*) (IV*a*) (0·8 g.), deep yellow needles, m. p. 198—200° (Found: C, 87·5; H, 4·7; N, 7·1%; *M*, 386. $C_{28}H_{26}N_2$ requires C, 87·5; H, 5·2; N, 7·3%; *M*, 384), $\lambda_{max.}$ 236, 308, and *358* mμ (ε 37,500, 33,000, and 10,500 in dioxan).

3-*Acetyl*-2-*methyl*-1-*phenylpyrrocoline* (III*c*).—(i) *From the alcohol.* 2-Methyl-1-phenyl-3-piperidino-1-2′-pyridylpropan-1-ol [3] (I*c*) (22 g.) and acetic anhydride (250 ml.) were boiled for 6 hr. After removal of excess of anhydride, addition of water gave a black viscous oil which partly solidified. This was extracted with boiling ether, leaving much black tar undissolved. The residue on evaporation of the ether was similarly extracted successively with light petroleum (b. p. 80—100°) and light petroleum (60—80°), with filtration each time (charcoal) from resin. The solid so obtained was recrystallised several times from light petroleum (b. p. 60—80°), to give acetylpyrrocoline (III*c*) (4·2 g.), m. p. 127—128°.

(ii) *From the alkenylamine.* The alcohol (I*c*) (60 g.) was dehydrated by storage in cold

concentrated sulphuric acid for 2 hr., and the alkenylamine separated [2] *via* the oxalates into pure *trans*-2-methyl-1-phenyl-3-piperidino-1-2′-pyridylprop-1-ene, *trans*-(II*c*), and substantially pure *cis*-(II*c*).

(a) The *trans*-alkenylamine (II*c*) (8·5 g.) was cyclised as described above. Addition of water gave an oil which solidified and was filtered off. The filtrate was basified and the liberated oil (A) isolated with ether. The solid was dissolved in ether, extracted several times with 2N-hydrochloric acid, and recovered as solid (B). The combined acid extracts were basified and the liberated oil was isolated with ether, combined with (A) (total, 5·5 g.) and distilled, the fraction having b. p. 142—150°/0·2 mm. being collected (3·7 g.). This solidified and recrystallised from light petroleum (b. p. 40—60°), to give *2-methyl-3-phenyl-3-2′-pyridylallyl acetate* (IX*c*) (2·5 g.), colourless plates, m. p. 64—65°, unchanged on admixture with the sample prepared from the *cis*-isomer (Found: C, 76·1; H, 6·3; N, 5·2; Ac, 16·1. $C_{17}H_{17}O_2N$ requires C, 76·4; H, 6·4; N, 5·2; Ac, 16·1%). The solid (B) on crystallisation from light petroleum (b. p. 60—80°) gave *3-acetyl-2-methyl-1-phenylpyrrocoline* (III*c*), large pale-yellow prisms, m. p. 127—128°. The acetate (IX*c*), on hydrolysis with 2N-hydrochloric acid and crystallisation of the crude product from light petroleum (b. p. 80—100°), gave *2-methyl-3-phenyl-3-2′-pyridylprop-2-en-1-ol* (X*c*), colourless needles or jagged prisms, m. p. 120° (Found: C, 80·0; H, 6·6; N, 6·0. $C_{15}H_{15}ON$ requires C, 80·0; H, 6·7; N, 6·2%).

(b) Alkenylamine (II*c*) (substantially *cis*-isomer) (42 g.), cyclised as in (a), gave the acetoxy-compound (IX*c*) (7·8 g.), m. p. 64—65°, unchanged on admixture with the sample prepared from the *trans*-isomer above, and acetylpyrrocoline (III*c*) (26·8 g.), m. p. 127—128°.

3-Acetyl-1-p-chlorophenyl-2-methylpyrrocoline (III*d*).—(i) *From the alcohol.* 1-*p*-Chlorophenyl-2-methyl-3-piperidino-1-2′-pyridylpropan-1-ol [2] (I*d*) (20 g.) and acetic anhydride (400 ml.) were boiled for 16 hr. Removal of excess of anhydride and addition of water gave a black tar (A) which was filtered off. The aqueous filtrate, on basification, gave an oil which was isolated with ether and distilled, to give 1-*p*-chlorophenyl-1-2′-pyridylprop-1-ene [1] (VIII*d*) (3·3 g.), b. p. 120—122°/0·1 mm. (Found: C, 72·5; H, 5·2; Cl, 15·7. Calc. for $C_{14}H_{12}NCl$: C, 73·2; H, 5·2; Cl, 15·5%). The solid (A) was cautiously washed free from black oil with acetone, and the solid residue crystallised from acetone to give acetylpyrrocoline (III*d*) (2·1 g.), m. p. 154°.

(ii) *From the alkenylamine.* The alcohol (I*d*) (88 g.) was dehydrated in concentrated sulphuric acid (500 ml.) for 2 hr. and the 1-*p*-chlorophenyl-2-methyl-3-piperidino-1-2′-pyridylprop-1-ene (II*d*) (85 g.) separated [2] *via* the oxalate into pure *trans*-(II*d*) (20 g.) and substantially pure *cis*-alkenylamines (II*d*) (68 g.). (*a*) The *trans*-isomer (20 g.) was cyclised by the standard method. Addition of water gave a sticky black solid. The aqueous filtrate was basified and the oil (A) (3 g.) isolated with ether. The black solid was washed with ether to give a friable solid (B). The ether filtrate was extracted several times with 2N-hydrochloric acid, the combined extracts were basified, and the separated oil was isolated with ether and freed from resinous material by dissolution in boiling light petroleum (b. p. 60—80°). The petroleum extract was evaporated to an oil (10 g.) which deposited some crystals. Filtration and washing with, followed by crystallisation from, light petroleum (b. p. 60—80°) gave colourless needles of the alkenol (X*d*) (1·3 g.), m. p. 113°, unchanged on admixture with the sample described below (Found: C, 69·1; H, 5·0; N, 5·5; Cl, 13·8%). The filtrate was combined with the oil (A) (total 11 g.) and distilled. The fraction having b. p. 175—180°/0·1 mm. (10 g.) was substantially the *acetoxy-compound* (IX*d*) (Found: Ac, 13·7. $C_{17}H_{16}O_2NCl$ requires Ac, 14·3%). It did not solidify and was hydrolysed by 2 hours' boiling with potassium hydroxide (22 g.) in water (22 ml.) and ethanol (100 ml.). Removal of the ethanol gave a crude solid which when washed and twice crystallised from light petroleum (b. p. 80—100°) gave *3-p-chlorophenyl-2-methyl-3-2′-pyridylprop-2-en-1-ol* (X*d*) (6·5 g.), colourless needles, m. p. 113—114°, unchanged on admixture with the sample prepared from the *cis*-isomer (Found: C, 69·7; H, 5·4; N, 5·4; Cl, 13·7. $C_{15}H_{14}ONCl$ requires C, 69·4; H, 5·4; N, 5·4; Cl, 13·7%). The solid (B) on crystallisation from ethanol gave *3-acetyl-1-p-chlorophenyl-2-methylpyrrocoline* (III*d*) (3·2 g.), cream-coloured needles, m. p. 155—156°. (*b*) The *cis*-isomer (68 g.) was cyclised as described above, to give: (i) the alkenol (X*d*) (0·6 g.), m. p. 113°; (ii) an oil, b. p. 180—184°/0·2 mm. (8 g.) (Found: Ac, 11·9%), which on hydrolysis gave the alkenol (X*d*) (3·5 g.), m. p. 113—114°, unchanged on admixture with the sample described above from the *trans*-isomer; and (iii) acetylpyrrocoline (III*d*) (45 g.), m. p. 153—154°, not depressed on admixture with the sample from the *trans*-isomer.

3-Acetyl-1 : 2-diphenylpyrrocoline (III*e*).—(i) *From the alcohol.* 1 : 2-Diphenyl-3-piperidino-1-2′-pyridylpropan-1-ol [2] (I*e*) (20 g.) and acetic anhydride (200 ml.) were boiled for 4 hr. Removal of acetic anhydride and addition of water gave a solid which was filtered off, washed with water and ethanol, and dried (13 g.). It was boiled with ethanol [520 ml.; sufficient to have dissolved the material had it all been acetylpyrrocoline (III*e*)] and filtered from material (A). The filtrate deposited crystals (10·2 g.) which after one further crystallisation from ethanol (charcoal) gave 3-acetyl-1 : 2-diphenylpyrrocoline (III*e*) (8·0 g.), straw-coloured needles, m. p. 175—176°. The solid (A) (2·5 g.) was recrystallised from acetone to give *di-(1 : 2-diphenyl-3-pyrrocolyl)methane* (VII*e*) (1·8 g.), fine pale needles, m. p. 250° (decomp.) (Found: C, 89·5; H, 5·4; N, 4·9. $C_{41}H_{30}N_2$ requires C, 89·5; H, 5·5; N, 5·1%).

(ii) *From the alkenylamine.* The alcohol (I*e*) (100 g.) was dehydrated in concentrated sulphuric acid (1 l.) at 0—10° for 24 hr. The 1 : 2-diphenyl-3-piperidino-1-2′-pyridylprop-1-ene (II*e*) (92 g.), crystallised from light petroleum (b. p. 40—60°) as described in Part VI,[2] gave a pure solid isomer (II*e*) (52 g.), m. p. 92—94°, and a semi-solid residue of mixed isomers.

(*a*) The solid isomer (II*e*) (50 g.) was cyclised by the standard method. After addition of water, a dark purple solid separated and was filtered off, washed, and dried (A; 45 g.). The aqueous filtrate was basified with ammonia, and the liberated oil isolated in ether. Evaporation of the ether gave oil (2·2 g.) which rapidly solidified. Crystallisation from light petroleum (b. p. 40—60°) gave two kinds of crystal. By repeated crystallisation (seeding in two places with the two sorts of crystal), separation of the deposited crystals by hand-picking, and recrystallisation of the separated fractions, were obtained a somewhat impure specimen of the acetoxy-compound (IX*e*) described below, compact prisms, m. p. 110—112°, and recovered alkenylamine (II*e*), rosettes of pointed prisms, m. p. and mixed m. p. 92—94° (Found: C, 84·7; H, 7·3; N, 7·7. Calc. for $C_{25}H_{26}N_2$: C, 84·7; H, 7·3; N, 7·9%). The solid A was lixiviated with cold ethanol (100 ml.) and recrystallised twice from boiling ethanol, to give acetylpyrrocoline (III*e*) (16 g.), m. p. 174—175°. The combined alcoholic filtrates were evaporated to a dark oil, which was dissolved in excess of 2N-hydrochloric acid, and filtered (charcoal); basification with ammonia gave oil which solidified and was filtered off, washed, and dried (23 g.). From this, after a prolonged series of crystallisations, were isolated: (i) 2 : 3-*diphenyl-3-2′-pyridylprop-2-en-1-ol* (X*e*) (7·4 g.), very soluble in ethanol and very sparingly soluble in hot light petroleum (b. p. 60—80°), but crystallising well from light petroleum (b. p. 80—100°), as needles, m. p. 120°, when crystallisation commenced while the solution was hot (Found: C, 83·9; H, 5·9; N, 4·8. $C_{20}H_{17}ON$ requires C, 83·6; H, 5·9; N, 4·9%) or jagged prisms, m. p. 126°, when crystallisation did not commence till the solution was cold (Found: C, 83·6; H, 5·9; N, 4·9%) (mixed m. p. of the two forms, 126°); (ii) 2 : 3-*diphenyl-3-2′-pyridylallyl acetate* (IX*e*) (9·8 g.), large prisms {from light petroleum (b. p. 60—80°) or from a small volume of ethanol [the latter effectively removing traces of the alkenol (X*e*)]}, m. p. 118° (Found: C, 80·1; H, 5·6; N, 4·6; Ac, 13·7. $C_{22}H_{19}O_2N$ requires C, 80·2; H, 5·8; N, 4·3; Ac, 13·1%).

(*b*) The residual mixed isomers (40 g.), cyclised as described under (*a*), gave acetylpyrrocoline (III*e*) (16·6 g.), m. p. 175—176°, the acetoxy-compound (IX*e*) (4·5 g.), m. p. 116—117° unchanged on admixture with the sample described above, and the alkenol (X*e*) (3·5 g.), a mixture of needles and prisms as described above.

Conversion of the Acetoxy-compound (IX*e*) *into the Chloro-compound* (XI*e*).—The acetoxy-compound (IX*e*) (2·0 g.) was heated in concentrated hydrochloric acid (30 ml.) on the steam-bath for 3 hr. Basification with ammonia and extraction with chloroform gave *3-chloro-1 : 2-diphenyl-1-2′-pyridylprop-1-ene*, large prisms [from light petroleum (b. p. 60—80°)], m. p. 123—124° (Found: C, 78·6; H, 5·3; N, 4·5; Cl, 11·6. $C_{20}H_{16}NCl$ requires C, 78·6; H, 5·2; N, 4·6; Cl, 11·6%).

3-Acetyl-1-p-chlorophenyl-2-phenylpyrrocoline (III*f*).—(i) 1-*p*-Chlorophenyl-2-phenyl-3-piperidino-1-2′-pyridylpropan-1-ol [2] (I*f*) (110 g.) was dehydrated in concentrated sulphuric acid at 0° for 24 hr., to give mixed isomers of 1-*p*-chlorophenyl-2-phenyl-3-piperidino-1-2′-pyridylprop-1-ene (II*f*) (102 g.). This (50 g.) was cyclised by the standard method. Addition of water gave a dark solid which was washed with ether and recrystallised twice from a large volume of ethanol (charcoal), to give *3-acetyl-1-p-chlorophenyl-2-phenylpyrrocoline* (III*f*) (21 g.), straw-coloured needles, m. p. 181—182°. The ether washings were extracted several times with 2N-hydrochloric acid, the combined acid extracts were basified with ammonia, and the liberated oil was isolated in ether and combined with the oil liberated from the original aqueous filtrate on basification. The ether layer, on evaporation, gave black tar (9·0 g.) which did not

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solidify when seeded with (III*f*) and was discarded. The basic oil (7·0 g.) rapidly solidified and was extracted several times with 200 ml. portions of boiling light petroleum (b. p. 60—80°). The combined extracts were evaporated to small volume and deposited crystals which, after further crystallisation from ethanol, followed by light petroleum (b. p. 60—80°), gave 3-p-*chlorophenyl*-2-*phenyl*-3-2′-*pyridylallyl acetate* (IX*f*) (4·5 g.), colourless rectangular prisms, m. p. 122° (Found: C, 72·4; H, 5·0; N, 4·0; Cl, 10·0; Ac, 11·8. $C_{22}H_{18}O_2NCl$ requires C, 72·6; H, 5·0; N, 3·9; Cl, 9·8; Ac, 11·8%).

(ii) Repetition of experiment (i) gave acetylpyrrocoline (III*f*) (16·0 g.), non-basic dark material (13 g.) from the ether layer after extraction with 2N-hydrochloric acid, and a dark basic oil (11·4 g.), which only partly solidified. From the latter, by repeated crystallisation from light petroleum (b. p. 80—100°) was obtained, not the acetoxy-compound (IX*f*), but 3-p-*chlorophenyl*-2-*phenyl*-3-2′-*pyridylprop*-2-*en*-1-*ol* (X*f*) (3·8 g.), colourless needles, m. p. 120° [mixed with (IX*f*), m. p. 100—108°] (Found: C, 75·1; H, 5·2; N, 4·2; Cl, 11·5. $C_{20}H_{16}ONCl$ requires C, 74·6; H, 5·0; N, 4·3; Cl, 11·0%).

3-*Methyl*-1-*phenylpyrrocoline* (V*g*).—(i) *From the alcohol.* 1-Phenyl-3-piperidino-1-2′-pyridylbutan-1-ol [2] (I*g*) (20 g.) and acetic anhydride (400 ml.) were boiled for 16 hr. After removal of excess of anhydride and addition of water, the separated oil was extracted with ether, and the ether layer washed several times with 2N-hydrochloric acid and evaporated to dryness. The residue was distilled, to give a yellow oil (2·6 g.), b. p. 160—175°/0·1 mm., which partially solidified, and on crystallisation from light petroleum (b. p. 40—60°) gave the pyrrocoline (V*g*) (0·8 g.), m. p. 67—68°, not depressed on admixture with the sample described below. The combined acid extracts on basification and ether-extraction gave an oil (9·8 g.) which, after distillation, was converted into its hydrochloride by ethereal hydrogen chloride. Crystallisation from chloroform–ether then gave 1-phenyl-1-2′-pyridylethylene hydrochloride [2] (VIII*g*), m. p. and mixed m. p. 187° (Found: C, 71·5; H, 5·5; N, 6·4; Cl, 16·0. Calc. for $C_{13}H_{12}NCl$: C, 71·7; H, 5·5; N, 6·4; Cl, 16·3%).

(ii) *From the alkenylamine.* The alcohol (I*g*) (50 g.) was dehydrated in concentrated sulphuric acid (500 ml.) at 0° for 6 hr. The 1-phenyl-3-piperidino-1-2′-pyridylbut-1-ene (II*g*) (42 g.) was cyclised by the standard method. Removal of excess of solvent and addition of water gave a brown oil which was extracted into ether, washed with dilute ammonia solution (to remove acetic acid), with water, and then with 2N-hydrochloric acid (4 × 200 ml.). The ether layer was evaporated and the residue (26 g.), crystallised from light petroleum (b. p. 40—60°), gave 3-*methyl*-1-*phenylpyrrocoline* (V*g*) (24 g.), golden-yellow plates, m. p. 67—68°. The combined acid extracts were basified, the oil isolated by means of ether, combined with the oil obtained by basifying the original aqueous filtrate, and distilled, to give a product (5·2 g.), b. p. 130—154°/0·2 mm., which was substantially the acetoxy-compound (IX*g*) (Found: Ac, 13·75. Calc. for $C_{17}H_{17}O_2N$: Ac, 16·1%).

1-p-*Chlorophenyl*-3-*methylpyrrocoline* (V*h*).—(i) *From the alkenylamine. cis*-1-*p*-Chlorophenyl-1-2′-pyridyl-3-pyrrolidinobut-1-ene (II*h*) (10 g.), separated from its *trans*-isomer by ion-exchange chromatography,[2] was cyclised by the standard method. After addition of water, yellow crystals separated which were filtered off, washed, and dried (7 g.), and on crystallisation from light petroleum (b. p. 40—60°) (charcoal) gave 1-p-*chlorophenyl*-3-*methylpyrrocoline* (V*h*) (4·5 g.), greenish-yellow lath-like plates, m. p. 91—92°. (ii) *From* 2-p-*chlorobenzylpyridine.* 2-*p*-Chlorobenzylpyridine [3] (10 g.) and propionic anhydride (60 ml.) were heated in a pressure tube at 280° for 8 hr. The liquid product was decanted from a little black solid, excess of anhydride removed *in vacuo*, and the residual oil washed with water and 2N-sodium hydroxide. Distillation gave 1-*p*-chlorophenyl-3-methylpyrrocoline (V*h*) (7·9 g.), b. p. 180—195°/0·5 mm., which solidified on being seeded and, crystallised from light petroleum (b. p. 40—60°), formed greenish-yellow plates (3·8 g.), m. p. and mixed m. p. 91°.

1 : 3-*Diphenylpyrrocoline* (V*i*).—(i) *From the alcohol.* 1 : 3-Diphenyl-3-piperidino-1-2′-pyridylpropan-1-ol [2] (I*i*) (5·0 g.) and acetic anhydride (50 ml.) were boiled for 6 hr. Removal of excess of anhydride and addition of water gave the pyrrocoline (V*i*) (2·1 g.), m. p. 115—116° (from ethanol). (ii) *From the alkenylamine.* The alcohol (I*i*) (50 g.) was dehydrated in ice-cold concentrated sulphuric acid (500 ml.) for 3 hr. The 1 : 3-diphenyl-3-piperidino-1-2′-pyridylprop-1-ene (II*i*) (47 g.) was cyclised by the standard method. 1 : 3-*Diphenylpyrrocoline* (V*i*) (26 g.) formed deep yellow needles, m. p. 115—116°, from alcohol. The aqueous filtrate from the reaction gave, on basification, an oil which after isolation by means of ether solidified

[3] Panizzon, *Helv. Chim. Acta*, 1944, **27**, 1748.

and on crystallisation from light petroleum (b. p. 40—60°) gave a *compound* (0·9 g.) as colourless prisms, m. p. 140—141° (Found: C, 84·9; H, 7·1; N, 7·7%; *M*, 341. $C_{25}H_{26}N_2$ requires C, 84·7; H, 7·3; N, 7·9%; *M*, 354), $\lambda_{max.}$ 260 and 265 mμ (ε 4800 and 4900 in EtOH). 1 : 3-Diphenyl-3-piperidino-1-2′-pyridylpropan-1-ol has $\lambda_{max.}$ 258 and 262 mμ (ε 4000 and 4000 in EtOH).

3-*Acetyl*-1-p-*methoxyphenylpyrrocoline* (XIV*a*).—1-*p*-Methoxyphenyl-1-2′-pyridyl-3-pyrrolidinopropan-1-ol [6] (XII*a*) (20 g.) was dehydrated in ice-cold 85% sulphuric acid (200 ml.) for 2 hr. The propene (XIII*a*) (16·5 g.) was cyclised by the standard method. Addition of water gave black, semi-solid material which was isolated, washed by decantation, and extracted with boiling light petroleum (b. p. 60—80°) (2 × 500 ml.). The petroleum-insoluble residue (A) consisted of yellow crystals mixed with much black tar. The petroleum filtrates were evaporated to give a yellow solid. A second extraction with light petroleum (b. p. 60—80°) (charcoal) and several crystallisations from ethanol and from acetone gave 3-*acetyl*-1-p-*methoxyphenylpyrrocoline* (XIV*a*) (4·5 g.), orange prisms, m. p. 122°. The material (A) was lixiviated with a little acetone, filtered off, and crystallised from pyridine, giving *di*-(1-p-*methoxyphenyl*-3-*pyrrocolyl*), yellow needles, m. p. 225°, $\lambda_{max.}$ 245, 266, 304, and *370* (ε 37,000, 31,000, 34,000, and 9000 in dioxan). No pyrrocoline was isolated when the alcohol (XII*a*) was boiled with acetic anhydride.

3-*Acetyl*-1-p-*tolylpyrrocoline* (XIV*b*).—The alcohol [3] (XII*b*) (40 g.) was dehydrated in ice-cold 85% sulphuric acid (400 ml.) for 3 hr. The propene (XIII*b*) (38 g.) was cyclised by the standard method. Addition of water gave dark solid which, on crystallisation from ethanol–light petroleum (b. p. 80—100°), afforded 3-*acetyl*-1-p-*tolylpyrrocoline* (XIV*b*), yellow plates, m. p. 133°. The original aqueous filtrate was basified with ammonia and extracted with ether, to give oil (5·0 g.) which was distilled; impure 3-2′-pyridyl-3-*p*-tolyl-allyl acetate (IX; R^1 = Me, R^2, R^3 = H) had b. p. 170—172°/0·5 mm. (Found: C, 77·5; H, 6·6; N, 4·9; Ac, 15·9. Calc. for $C_{17}H_{17}O_2N$: C, 76·4; H, 6·4; N, 5·2; Ac, 16·1%).

3-*Acetyl*-1-o-*tolylpyrrocoline* (XIV*c*).—1-2′-Pyridyl-3-pyrrolidino-1-*o*-tolylpropan-1-ol [3] (XII*c*) (26 g.) was dehydrated in 85% sulphuric acid (260 ml.) on the steam-bath for 20 min. The propene (19 g.) was separated [3] by ion-exchange chromatography into the *trans*- (XIII*c*) (8·1 g.) and the *cis*-isomer (XIII*c*) (10·2 g.). (i) The *trans*-isomer (8·1 g.) was cyclised by the standard method. Addition of water gave a dark oil which was isolated with ether and distilled (b. p. 158—162°/0·1 mm.) as an oil (3·5 g.). This, on crystallisation from light petroleum (b. p. 60—80°), gave a *compound* (Q) (1·2 g.) as large colourless prisms, m. p. 114° (Found: C, 81·9; H, 6·0; O, 6·7; N, 5·7%; Ac, 0; reduction, 1·05 double bond calc. on *M* 250. $C_{17}H_{15}ON$ requires C, 81·9; H, 6·0; O, 6·4; N, 5·6%), $\lambda_{max.}$ 258, 264, 321, and 330 mμ (ε 4610, 4660, 261, 266 in EtOH); after reduction $\lambda_{max.}$ were at 263, *268*, 296, and 305 (ε 4300, 3500, 270, and 280 in EtOH). (ii) The *cis*-isomer (10·2 g.), on cyclisation and addition of water, gave an oil, b. p. 180—184°/0·2 mm. (7·1 g.), which set to a glass. Crystallisation from light petroleum (b. p. 60—80°) gave a mixture (5·7 g.) of colourless and pale yellow crystals from which the colourless material was eluted in 2N-hydrochloric acid. The insoluble yellow 3-*acetyl*-1-o-*tolylpyrrocoline* (XIV*c*) crystallised from light petroleum (b. p. 40—60°) as pale yellow prisms (4·4 g.), m. p. 65°. From the acid washings, by basification and crystallisation from light petroleum (b. p. 60—80°), was obtained compound (Q) (0·4 g.), m. p. 112—113°.

3-*Acetyl*-8-*methyl*-1-*phenylpyrrocoline* (XIV*d*).—1-(3-Methyl-2-pyridyl)-1-phenyl-3-pyrrolidinoprop-1-ene [3] (XIII*d*) (5·5 g.) was cyclised by the standard method. Addition of water gave a dark oil which was extracted into ether. The ether layer was washed with 2N-hydrochloric acid, water, and dilute aqueous ammonia, filtered (charcoal), and evaporated (3·0 g.). Crystallisation from light petroleum (b. p. 40—60°) gave 3-*acetyl*-8-*methyl*-1-*phenylpyrrocoline* (XIV*d*), large straw-coloured prisms (2·2 g.), m. p. 100—101°.

3-*Acetyl*-1-p-*chlorophenyl*-8-*methylpyrrocoline* (XIV*e*).—1-*p*-Chlorophenyl-1-(3-methyl-2-pyridyl)-3-pyrrolidinopropan-1-ol [3] (XII*e*) (30 g.) was dehydrated in 85% sulphuric acid (150 ml.) on the steam-bath for 10 min. The propene (XIII*e*) was separated [3] *via* the oxalates into *cis*- (XIII*e*) (16 g.) and substantially pure *trans*-propene (XIII*e*) (12 g.).

The *cis*-propene (16 g.) was cyclised by the standard method. Addition of water precipitated a dark solid (14·8 g.) which, on crystallisation from acetone, then from light petroleum (b. p. 60—80°), gave the *pyrrocoline* (XIV*e*) (10·6 g.), as large, almost colourless prisms, m. p. 112—113°. The *trans*-isomer (12 g.) gave no pyrrocoline.

3-*Acetyl*-1-(5-*chloro*-2-*thienyl*)*pyrrocoline* (XIV*f*).—1-(5-Chloro-2-thienyl)-1-2′-pyridyl-3-pyrrolidinopropan-1-ol [6] (XII*f*) (5 g.) was dehydrated in 65% sulphuric acid on the steam-bath

for 15 min. The propene (XIII*f*) (4·5 g.) was cyclised by the standard method. Addition of water gave a semisolid black mass, which was filtered off and extracted with ether (Soxhlet). Evaporation of the ether gave a dark solid (2·5 g.), then by two crystallisations from light petroleum (b. p. 60—80°) yellow crystals. Two crystallisations from ethanol [with filtration the first time from yellow material (A)] gave **3-*acetyl*-1-(5-*chloro*-2-*thienyl*)*pyrrocoline*** (XIV*f*) as rosettes of yellow needles, m. p. 119°. The material (A), m. p. 217—220°, was probably di-[1-(5-chloro-2-thienyl)-3-pyrrocolyl], $\lambda_{max.}$ 234, *250*, 330, *370* (ε 26,000, 23,500, 25,900, 11,000 in EtOH). Heating the alcohol (XII*f*) with acetic anhydride gave no pyrrocoline.

3-*Acetyl*-1-2′-*pyridylpyrrocoline* (XIV*g*).—3-Dimethylamino-1 : 1-di-2′-pyridylpropan-1-ol [6] (XII*g*) (10 g.) and acetic anhydride (200 ml.) were boiled for 6 hr. After removal of anhydride, addition of water precipitated a black solid which, after several crystallisations from light petroleum (b. p. 60—80°), gave **3-*acetyl*-1-2′-*pyridylpyrrocoline*** (XIV*g*), yellow plates, m. p. 112°.

***Di*-(1-*phenyl*-3-*pyrrocolyl*)**.—The alkenylamine (II*a*) (10 g.) was dissolved in chloroform, and 50% aqueous hydrobromic acid (4·4 ml.) was added. The chloroform was removed. The hydrobromide crystallised and was heated with quinoline (50 ml.) at 160° for 3 hr. The quinoline was removed by distillation and steam-distillation and the dark residue dissolved in ether; Filtration, evaporation, and storage overnight afforded crystals. These were washed with acetone and recrystallised from light petroleum (b. p. 60—80°), to give the dipyrrocolyl (IV*a*) (0·2 g.), m. p. and mixed m. p. 189—192°, $\lambda_{max.}$ 236, 310, and *358* (ε 35,100, 30,800, and 9600 in dioxan).

***Di*-(1-p-*chlorophenyl*-3-*pyrrocolyl*)**.—(i) The *trans*-alkenylamine (II*b*) (10 g.), quinoline (40 ml.), and 50% aqueous hydrobromic acid (5 ml.) were heated at 160° for 3 hr. During three days' storage crystals separated and were filtered off, washed with ethanol, and dried (1·2 g.). Crystallisation from pyridine gave the dipyrrocolyl (IV*b*), m. p. and mixed m. p. 285—288°. (ii) The *cis*-alkenylamine (II*b*) (10 g.) similarly reacted to give the dipyrrocolyl (IV*b*) (1·1 g.).

1-2′-*Pyridylindan*-1-*ol*.—Indan-1-one was treated with pyridyl-lithium as described in Part III,[6] to give **1-2′-*pyridylindan*-1-*ol***, b. p. 158—165°/0·3 mm., prisms from light petroleum (b. p. 40—60°), m. p. 78—79° (Found: C, 79·9; H, 6·2; N, 6·4. $C_{14}H_{13}ON$ requires C, 79·6; H, 6·2; N, 6·6%), $\lambda_{max.}$ 262 (ε 5400 in EtOH).

3-2′-*Pyridylindene*.—The indanol (2 g.) was dehydrated in 85% sulphuric acid (20 ml.) at 0° for 2 hr. Crystallisation from light petroleum (b. p. 40—60°) gave the ***indene*** as colourless needles or prisms, m. p. 80—82° (depressed to 55—58° on admixture with the indanol) (Found: C, 87·3; H, 5·7; N, 7·1. $C_{14}H_{11}N$ requires C, 87·0; H, 5·7; N, 7·3%), $\lambda_{max.}$ 235 and 280 (ε 21,000 and 6500 in EtOH).

1-*Arylpyrrocolines*.—3-Acetyl-1-phenylpyrrocoline (III*a*) (2·6 g.) was boiled with concentrated hydrochloric acid (30 ml.) till the initial orange colour disappeared (*ca.* 5 min.). The mixture was cooled and basified, and the liberated oil extracted with ether and distilled. The fraction boiling at 155—160°/0·3 mm. crystallised from light petroleum (b. p. 40—60°), to give **1-*phenylpyrrocoline*** (V*a*), pale yellow prisms, m. p. 68°. The **1-*arylpyrrocolines*** given in Table 2 were prepared similarly. They decomposed rapidly on exposure to air and light. Analytical samples were prepared in most cases by sublimation at 0·1—0·5 mm.

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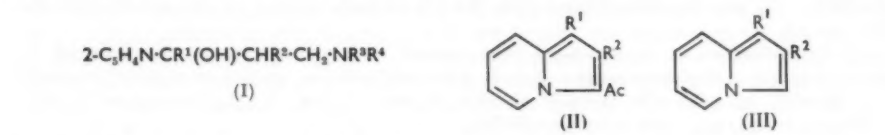
63. *Aminoalkyl Tertiary Carbinols and Derived Products. Part VIII.*[1] *Some* 1-*Alkyl- and* 1 : 2-*cyclo*Alkano-*pyrrocolines.*

By P. A. Barrett and (the late) K. A. Chambers.

1-(Tertiary amino)-3-2′-pyridylalkan-3-ols (I) and 1 : 5-di(tertiary amino)-3-2′-pyridylalkan-3-ols (V) have been cyclised to the corresponding 1-alkyl- and 1-2′-(tertiary amino)alkyl-pyrrocolines (II) and (VI). The analogous *cyclo*alkanols (X) are shown to be mixtures containing more than one of the possible steroisomers. The isomers present in larger amount give no pyrrocoline on cyclisation and are assigned the all-*trans*-configuration. The other isomers cyclise to the corresponding tricyclic 3-acetylpyrrocolines (XIV) and contain at least one *cis*-grouping.

In Part VII [1] was described a new synthesis of 1-arylpyrrocolines, *e.g.*, (II; $R^1 = Ph$, $R^2 = H$), from the corresponding 3-(tertiary amino)-1-aryl-1-2′-pyridylpropan-1-ols, *e.g.*, (I; $R^1 = Ph$, $R^2 = H$, $NR^3R^4 = N<[CH_2]_4$), in acetic anhydride. We now describe the extension of this reaction to the preparation of some 1-alkyl- and 1 : 2-*cyclo*alkano-pyrrocolines.

A series of alkanols (I; R^1 = alkyl, R^2 = H or alkyl) (Table 1) was prepared from 2-pyridyl-lithium and the appropriate 1-(tertiary amino)alkan-3-ones and cyclised by boiling acetic anhydride to the corresponding acetylpyrrocolines (II; R^1 = alkyl, R^2 = H or alkyl). Reaction was slower and cleaner, and the yield higher, than in the cyclisations to 1-arylpyrrocolines described in Part VII,[1] and formation of the corresponding



Compounds I—III	R^1	R^2	R^3R^4	Compounds I—III	R^1	R^2	R^3R^4
a	Me	H	$<[CH_2]_5$	*f*	Me	$CH_2·NEt_2$	Et_2
b	Et	Me	Me_2	*g*	Me	$CH_2·N<[CH_2]_5$	$<[CH_2]_5$
c	Pr	Et	Me_2				
d	Me	Me	Me_2				
e	CMe_3	H	$<[CH_2]_5$				

dipyrrocolylmethanes has not been observed. It is concluded that the alkyl-carbinols undergo to a much smaller extent, if at all, reaction by the alternative route encountered [1] in the aryl series. The 3-acetyl-1-alkylpyrrocolines (II*a* and *d*) are stable yellow solids, hydrolysed to the 1-alkylpyrrocolines (III*a* and *d*), which, though readily obtained pure by vacuum-sublimation,[2] were markedly less stable to exposure than the corresponding 1-arylpyrrocolines. The alkylpyrrocolines (III*b*, *c*, and *e*) were oils.

Reaction of 2-pyridyl-lithium with the symmetrical 1 : 5-bisdimethylaminoalkan-3-ones (IV*a*) and (IV*b*) gave the 1 : 5-bisdimethylamino-3-2′-pyridylalkan-3-ols (V*a*) and (V*b*). These on cyclisation gave the 3-acetyl-1-dimethylaminoalkylpyrrocolines, one of which (VI*a*) was an oil, characterised as the hydrogen oxalate, and the other (VI*b*) was solid. The unsymmetrical 1 : 5-bisdimethylaminoalkan-3-ones (IV*c*) and (IV*d*) similarly gave the 2′-pyridylalkanols (V*c* and *d*), which on cyclisation gave high yields of the 3-acetyl-1-dimethylaminoalkylpyrrocolines (VI*c* and *d*): these pyrrocolines may be either of two isomers, or a mixture of both, depending on the relative proportions of the two non-equivalent amino-groups participating in the cyclisation. Analysis and ultraviolet absorption spectra confirm their formulation as (VI*c* and *d*) but attempts to separate them into pure isomers by base-exchange chromatography or by fractional crystallisation of

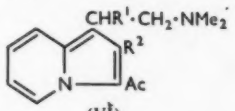
[1] Part VII, preceding paper.
[2] Cf. Holland and Naylor, *J.*, 1955, 1657.

their oxalates were unsuccessful. Regardless of which isomer preponderates in the mixture, the isolation of the pyrrocoline (VI*c*) in high yield establishes unequivocally as (IV*c*) the constitution of the di-Mannich base from ethyl methyl ketone, which has long been uncertain. Cardwell [3] rigorously proved the structure of the mono-Mannich base from ethyl methyl ketone and preferred, without proof, the structure (IV*c*) for the di-Mannich base. Haeussler and Schacht,[4] however, assigned the compound the structure (VIII*a*) on the basis of an iodoform reaction. Only if this compound has the constitution (IV*c*) can the derived 2-pyridylcarbinol give a pyrrocoline on cyclisation. The 2-pyridylcarbinol from (VIII*a*) would be precluded from doing so by the presence of the quaternary carbon atom.

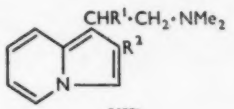
From one preparation of the pentanol (V*a*) of wide boiling range there was isolated after cyclisation, in addition to acetylpyrrocoline (II*a*), a compound to which on the basis of analysis and ultraviolet spectrum is assigned the constitution (II; $R^1 = Me$, $R^2 = OAc$). Presumably this was formed from unsymmetrical dipiperidinoalkanol (I*g*) present as a contaminant of the butanol (I*a*), with subsequent deamination. Analogous deamination during cyclisation has been encountered in the *cyclo*alkanol series (see below). However, after the cyclisation of the pure di(tertiary amino)alkanols (I*f*) and (I*g*) no pyrrocoline derivatives could be isolated.

$NMe_2 \cdot CH_2 \cdot CHR^1 \cdot CO \cdot CHR^2 \cdot CH_2 \cdot NMe_2$ (IV)

$NMe_2 \cdot CH_2 \cdot CHR^1 \cdot C(C_5H_4N\text{-}2)(OH) \cdot CHR^2 \cdot CH_2 \cdot NMe_2$ (V)



(VI)



(VII)

Compounds IV—VII	R^1	R^2		R^1	R^2
a	H	H			
b	Me	Me			
c	H	Me	*or*	Me	H
d	H	Et	*or*	Et	H

$Me \cdot CO \cdot CR^1(CH_2 \cdot NR^2R^3)_2$ (VIII): *a* $R^1 = Me$, $R^2R^3 = Me_2$
b $R^1 = H$, $R^2R^3 = <[CH_2]_5$
c $R^1 = H$, $R^2R^3 = Et_2$

The present reaction is among the few pyrrocoline syntheses in which the complete carbon skeleton is present in one stable molecule before cyclisation. This permits the preparation of pyrrocoline derivatives, otherwise doubtfully accessible, which carry additional fused cyclic structures. The 2-pyridylcarbinol (X*b*), prepared from the *cyclo*hexanone Mannich base (IX*b*), on cyclisation (6 hr.) gave a low yield of the tricyclic pyrrocoline derivative (XIV*b*) and a high yield of the acetate (XI*b*). The alcohol (X*b*) derived from the latter by hydrolysis gave no pyrrocoline but was quantitatively reconverted into acetate (XI*b*) on treatment (12 hr.) with acetic anhydride. In Part VII [1] the difference in behaviour of *cis*- and *trans*-3-(tertiary amino)-1-aryl-1-2′-pyridylprop-1-enes * towards acetic anhydride was interpreted in terms of a sharp distinction between the *cis*-isomer giving pyrrocoline, and the *trans*-isomer giving none, confused by a slow isomerisation. In the present case we deduce that the recovered acetate (XI*b*) and the alcohol (X*b*) derived from it, neither of which gave pyrrocoline (XIV*b*) on treatment with acetic anhydride, have the *trans*-configuration, and that the alcohol (X*b*) as prepared was a mixture containing about 25% of the *cis*-isomer which was removed during the first treatment with acetic anhydride with formation of the pyrrocoline (XIV*b*). In contrast to the alkenylamines,[1] the difference in behaviour is sharp because the possibility of

* *cis* and *trans* refer to the relation of the pyridine and the aminomethyl group.

[3] Cardwell, *J.*, 1950, 1056.
[4] Haeussler and Schacht, *Ber.*, 1950, **83**, 129.

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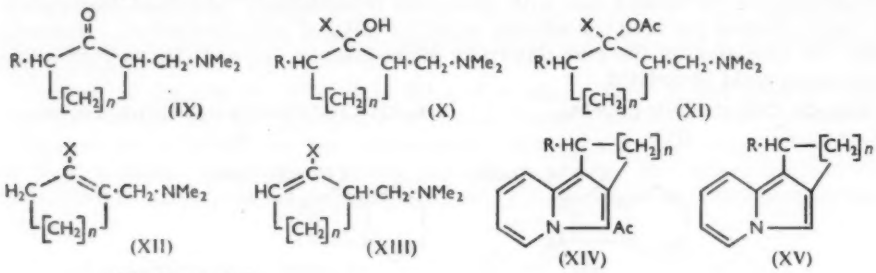
isomerisation is excluded. This interpretation is confirmed by additional examples described below. In connection with the relation between configuration and ability to cyclise it is noteworthy that neither 4-hydroxy-1-methyl-4-2′-pyridylpiperidine (XVI) nor the derived 1 : 2 : 5 : 6-tetrahydro-1-methyl-4-2′-pyridylpyridine (XVII), both of which may be regarded as extreme *trans*-forms of their respective types of isomerism, gave a pyrrocoline derivative on submission to cyclisation.

The *trans*-alcohol (X*b*) gave on dehydration a mixture of *cyclo*alkenes (XII*b*) and (XIII*b*) which was separated into a solid and a liquid fraction through the insolubility of the oxalate of the former. On treatment with acetic anhydride the solid was recovered unchanged, while the liquid fraction gave a 25% yield of the tricyclic pyrrocoline derivative (XIV*b*). It is concluded that the latter was substantially 2-dimethylaminomethyl-1-2′-pyridyl*cyclo*hex-1-ene (XII*b*) which, being a substituted *cis*-3-aminoprop-1-ene, should give a high yield of the corresponding pyrrocoline on cyclisation, and that the solid was the corresponding *cyclo*hex-6-ene (XIII*b*).



X = 2-pyridyl

IX—XV	R	*n*	IX—XV	R	*n*
a	H	2	*e*	$CH_2·NMe_2$	3
b	H	3	*f*	$CH_2·NMe_2$	4
c	H	4	*g*	$CH_2·OAc$	3
d	$CH_2·NMe_2$	2	*h*	$CH_2·OAc$	4

Analogous behaviour was observed in the corresponding compounds from *cyclo*pentanone. Small yields of identical pyrrocoline (XIV*a*) were isolated on cyclisation both from the mixed isomeric *cyclo*pentanols (X*a*) and from the mixed *cyclo*pentenes (XII*a*) and (XIII*a*), the product of dehydration of the *trans*-alcohol obtained by hydrolysis of the *trans*-acetate (XI*a*) recovered from the cyclisation of the total alcohol. No attempt was made to separate the isomeric *cyclo*pentenes (XII*a*) and (XIII*a*).

The corresponding *cyclo*heptanol (X*c*) gave on cyclisation a small yield of non-basic oil, shown by ultraviolet absorption spectrum to contain some pyrrocoline (which was however not obtained pure) and the solid *trans*-acetate (XI*c*). Dehydration of the heptanol was not investigated.

The bis(dimethylaminomethyl)-2′-pyridyl*cyclo*alkanols (X*d*, *e*, and *f*) have been prepared from the corresponding bis(dimethylaminomethyl)*cyclo*alkanones (IX*d*, *e*, and *f*). The possibility that the latter are the unsymmetrical αα-disubstituted *cyclo*alkanones has not been rigorously disproved. However, no evidence was found to suggest that they were heterogeneous, and all the evidence available (cf. refs. 2, 5, 6, and see above) shows that aminomethylation occurs preferentially at a secondary rather than at a primary carbon atom, and at a primary rather than at a tertiary carbon atom. Further, the Mannich base from 2-methyl*cyclo*hexanone has been shown [7] to be 2-dimethylaminomethyl-6-methyl-*cyclo*hexanone and not the 2 : 2-compound. The bis(dimethylaminomethyl)*cyclo*alkanones are therefore assigned the constitution (IX), and the derived alcohols the constitution (X).

[5] Blicke in "Organic Reactions," Vol. I, Chapman and Hall, London, 1942, p. 303.
[6] Wilds and Shunk, *J. Amer. Chem. Soc.*, 1943, **65**, 469.
[7] de Feu, McQuillin, and Robinson, *J.*, 1937, 53.

TABLE 1. *1-(Tertiary amino)- and 1 : 5-di(tertiary amino)-3-2′-pyridylalkan-3-ols (I) and (V).*

Compound	R^1	R^2	R^3R^4	B. p./mm.	M. p.[a]	Formula	Found (%) C	H	N	Required (%) C	H	N

TABLE 1. 1-(*Tertiary amino*)- *and* 1 : 5-*di*(*tertiary amino*)-3-2′-*pyridylalkan*-3-*ols* (I) *and* (V).

Compound	R^1	R^2	R^3R^4	B. p./mm.	M. p.[a]	Formula	Found (%) C	Found (%) H	Found (%) N	Required (%) C	Required (%) H	Required (%) N
I*a*	Me	H	$<[CH_2]_5$	120—122°/0·5	—	$C_{14}H_{22}ON_2$	71·5	9·5	12·2	71·8	9·4	12·0
I*b*	Et	Me	Me_2	99—100/0·2	—	$C_{13}H_{22}ON_2$	70·1	9·6	12·6	70·3	9·9	12·6
I*c*	Pr	Et	Me_2	125—128/0·5	—	$C_{15}H_{26}ON_2$	72·3	10·7	11·1	72·0	10·5	11·2
I*d*	Me	Me	Me_2	98—100/0·3	—	$C_{12}H_{20}ON_2$	69·0	9·6	13·2	69·2	9·6	13·5
I*d*	Me	Me	$<[CH_2]_5$	132—134/0·3	—	$C_{15}H_{24}ON_2$	72·0	9·6	11·3	72·5	9·7	11·3
I*e*	CMe_3	H	$<[CH_2]_5$	140—150/0·5	79—81°	$C_{17}H_{28}ON_2$	74·3	10·1	10·3	74·0	10·1	10·1
I*f*	Me	$CH_2{\cdot}NEt_2$	Et_2	150—155/1·5	—	$C_{16}H_{28}ON_2$	70·3	10·6	13·2	70·4	10·7	13·7
I*g*	Me	$CH_2{\cdot}N<[CH_2]_5$	$<[CH_2]_5$	186—190/0·2	—	$C_{20}H_{32}ON_2$	73·2	9·8	12·2	72·5	10·0	12·7
V*a*	H	H	—	138—142/0·5	73—74	$C_{14}H_{22}ON_2$	67·2	10·1	16·8	67·0	10·1	16·7
V*b*	Me	Me	—	130—140/0·4	98—99	$C_{16}H_{26}ON_2$	69·2	10·0	15·1	68·7	10·4	15·1
V*c*	Me	H	—	130—135/0·3 [*]	—	$C_{15}H_{24}ON_2$	68·4	9·9	14·6	67·9	10·2	15·8
V*d*	Et	H	—	130—132/0·2	—	$C_{16}H_{26}ON_2$	69·4	10·2	14·1	68·7	10·4	15·1
[*] Oxalate, recryst. from ethanol					156	$C_{19}H_{31}O_9N_3$	51·0	7·3	—	51·3	7·0	—

[a] After crystallisation from light petroleum (b. p. 40—60°).

TABLE 2. 3-*Acetyl*-1-*alkylpyrrocolines and* 3-*acetyl*-1-2′-*(tertiary amino)alkylpyrrocolines* (II *and* VI).

Compound	R^1	R^2	B. p./mm.	M. p.	Formula	Found (%) C	Found (%) H	Found (%) N	Required (%) C	Required (%) H	Required (%) N
II*a*	Me	H	140—150°/0·2	100—101° [a]	$C_{11}H_{11}ON$	76·6	6·5	8·3	76·4	6·4	8·1
II*b*	Et	Me	140—148/0·1	82 [a]	$C_{13}H_{15}ON$	77·2	7·5	7·0	77·6	7·5	7·0
II*c*	Pr	Et	160—170/0·5	51—52 [b,c]	$C_{15}H_{19}ON$	78·6	8·4	6·1	78·6	8·3	6·1
II*d*	Me	Me	140—145/0·3	99—100 [a]	$C_{13}H_{15}ON$	77·3	6·8	7·6	77·0	7·0	7·5
II*e*	CMe_3	H	—	108—109 [b]	$C_{14}H_{17}ON$	78·0	8·0	6·3	78·2	7·9	6·5
VI*a*	H	H	165—175/0·5	—	—	—	—	—	—	—	—
,,	,,	,,	—	100 [d]	$C_{14}H_{19}ON_3,C_2H_2O_4,H_2O$	56·8	6·5	8·6	56·8	6·5	8·3
,,	,,	,,	—	176—177 [e]	$C_{16}H_{19}ON_2,C_2H_2O_4$	59·3	6·2	8·8	60·0	6·3	8·8
VI*b*	Me	Me	160—164/0·5	72 [b]	$C_{16}H_{22}ON_2$	74·7	8·3	11·0	74·5	8·5	10·9
,,	,,	,,	—	178 [f]	$C_{16}H_{22}ON_2,C_2H_2O_4$	62·2	6·7	8·1	62·1	6·9	8·1
VI*c*	H or Me	Me or H	152—158/0·1	—	$C_{15}H_{20}ON_2$	73·4	8·2	11·3	73·8	8·2	11·5
,,	,,	,,	—	175—177 [f]	$C_{15}H_{20}ON_2,C_2H_2O_4$	60·7	6·7	8·6	60·7	6·6	8·4
VI*d*	H or Et	Et or H	160—170/0·2	—	$C_{16}H_{22}ON_2$	—	—	10·8	—	—	10·9
,,	,,	,,	—	152—157 [f]	$C_{16}H_{22}ON_2,C_2H_2O_4$	62·4	7·0	8·2	62·1	6·9	8·1

[a, b] Cryst. from light petroleum ([a] b. p. 60—80°; [b] b. p. 40—60°). [c] Sublimed *in vacuo*. [d] Monohydrate (from H_2O). [e] Anhydr. (dried at 100°) Cryst. from EtOH–Et_2O.

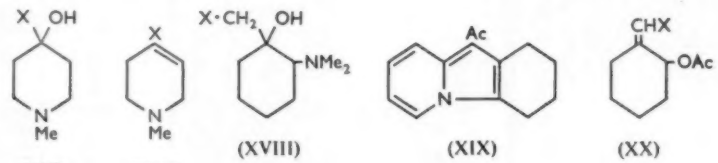
TABLE 2*a*.

Compound [a]	Absorption max. in EtOH: λ (mμ)					ε				
II*a*	227	—	266	370	383	16,200	—	24,500	15,700	14,300
II*b*	231	256	275	370	382	21,900	12,200	24,000	13,900	12,800
II*c*	232	258	276	373	386	23,000	12,800	23,000	14,000	12,700
II*d*	230	255	275	372	384	20,000	11,500	24,000	13,700	12,800
II*e*	266	240 [*]	264	370	380	17,500	9,000	24,000	16,000	14,500
VI*a*	225	—	262	364	—	16,000	—	19,000	11,000	—
VI*b*	230	—	276	370	—	21,000	—	22,000	13,000	—
VI*c*	230	—	266	268	—	18,000	—	22,000	13,600	—
VI*d*	228	—	265	268	—	19,000	—	20,000	13,500	—

[*] Inflexion. [a] Examined as base, except (VI*a*) as anhydrous oxalate.

The substituted *cyclo*hexanol (X*e*), as prepared, was a mixture of isomers, one of which was isolated as its solid acetate (XI*e*). This gave no pyrrocoline on long boiling with acetic anhydride. The bulk was recovered unchanged though some deamination occurred with the production of the high-melting, well characterised, diacetate (XI*g*). Both these compounds are assigned the *trans-trans*-configuration. The oily residue left after separation of the solid acetate (XI*e*) gave on cyclisation a moderate yield of the dimethylaminomethylpyrrocoline (XIV*e*). This material therefore contained *cyclo*hexanol (X*e*) having some *cis*-configuration. From cyclisations carried out on the total alcohol, as prepared, the same three compounds have been isolated. The yields of pyrrocoline (XIV*e*) from different samples varied, however, suggesting variation in the proportion of stereoisomers in the *cyclo*hexanol (X*e*).

The substituted *cyclo*heptanol (X*f*) formed a semisolid mixture from which two of the three possible stereoisomers have been isolated, having m. p.s 84° and 82° respectively (mixed m. p. 56°). Both gave solid acetates (XI*f*) (m. p. 89° and 87° respectively; mixed m. p. 60°). The acetate (m. p. 87°) was recovered unchanged after long boiling with acetic anhydride, and is assigned the *trans-trans*-configuration. The acetate (m. p. 89°) gave on cyclisation a 50% yield of the dimethylaminomethylpyrrocoline (XIV*f*) and a



(XVI) (XVII) (XVIII) (XIX) (XX)

X = 2-pyridyl $2\text{-}C_5H_4N\cdot CH_2\cdot CPh(OH)\cdot CH_2\cdot N\langle[CH_2]_5$ (XXI)

5% yield of the acetoxymethylpyrrocoline (XIV*h*). This acetate is assigned the *cis-trans*-configuration. In all the alcohols examined the isomer having exclusively *trans*-configuration has been present in greater amount, and it seems probable that the isomer next in abundance will have the *cis-trans*- and not the *cis-cis*-configuration. In one experiment the solid portion of the crude alcohol gave the pure *cis-trans*-isomer. The solid isolated in later preparations was always a mixture of the two isomers. These were converted into the acetates (XI*f*), and the latter separated by fractional crystallisation of their oxalates.

The corresponding diamino*cyclo*pentanol (X*d*), submitted to cyclisation, gave material shown by the absorption spectrum to contain some pyrrocoline derivative, but this could not be characterised.

Cyclisation to a substituted pyrrocoline is not limited to 1-2′-pyridylpropan-1-ols but can occur with 1-2′-pyridylpropan-2-ols. This has been shown with 2-dimethylamino-1-(2′-pyridylmethyl)*cyclo*hexanol (XVIII) which on cyclisation gave 10-acetyl-1 : 2 : 3 : 4-tetrahydrobenzo[*b*]pyrrocoline (XIX). Deamination led simultaneously to a compound for which the analysis and ultraviolet spectrum suggest the constitution (XX). From the attempted cyclisation of 3-piperidino-2-phenyl-1-2′-pyridylpropan-2-ol (XXI), however, no pyrrocoline derivative could be isolated.

Experimental

Light-absorption data refer to EtOH solution.

Mono- and Di-β-(tertiary amino)alkanones.—Ketones were prepared by published methods,[3, 7–10] except the following.

1-*Dimethylamino*-2-*ethylhexan*-3-*one*, prepared by the Mannich reaction[9] from di-*n*-propyl

[8] (*a*) Mannich and Hof, *Arch. Pharm.*, 1927, **265**, 589; (*b*) Hagemeyer, *J. Amer. Chem. Soc.*, 1949, **71**, 1119.
[9] Mannich, *Arch. Pharm.*, 1917, **255**, 261.
[10] Mannich and Hof, *ibid.*, 1926, **264**, 749.

XUM

ketone, had b. p. 104°/12 mm. (Found: C, 70·2; H, 12·1; N, 8·5. $C_{10}H_{21}ON$ requires C, 70·2; H, 12·3; N, 8·2%).

1 : 5-*Bisdimethylamino*-2-*ethylpentan*-3-*one*, prepared by the method of Mannich and Hof,[10] had b. p. 117—120°/12 mm. (Found: C, 65·7; H, 11·7; N, 13·5. $C_{11}H_{24}ON_2$ requires C, 66·0; H, 12·0; N, 14·0%). The *dihydrochloride* (from methanol) had m. p. 166—167° (Found: C, 48·0; H, 9·4; N, 10·1; Cl, 25·1. $C_{11}H_{26}ON_2Cl_2$ requires C, 48·4; H, 9·6; N, 10·3; Cl, 26·0%).

1 : 1-Bisdiethylaminomethylpropan-2-one (VIII*c*) was prepared by the method of Wilds and Shunk.[6] 1 : 1-*Bispiperidinomethylpropan*-2-*one* (VIII*b*), similarly prepared, had b. p. 175—180°/15 mm. (Found: C, 69·4; H, 11·2; N, 10·9. $C_{15}H_{28}ON_2$ requires C, 71·5; H, 11·2; N, 11·2%). An attempt to prepare the bisdimethylamino-analogue by this method failed.

2-*Dimethylaminomethyl*cyclo*alkanones*.—2-Dimethylaminomethyl*cyclo*hexanone was prepared by Frank and Pierle's method.[11] It was necessary to use slow addition and very vigorous stirring if substantial simultaneous production of the di-Mannich base (see below) was to be avoided.

2-*Dimethylaminomethyl*cyclo*pentanone*, prepared similarly from *cyclo*pentanone, had b. p. 95—96°/15 mm., n_D^{21} 1·4580 (Found: C, 68·2; H, 10·6; N, 9·7. $C_8H_{15}ON$ requires C, 68·1; H, 10·6; N, 9·9%). The *hydrochloride*, plates from ethanol–ether, had m. p. 147—148° (Found: C, 53·8; H, 8·9; N, 7·7; Cl, 20·7. $C_8H_{16}ONCl$ requires C, 54·0; H, 9·0; N, 7·9; Cl, 20·0%). The *methiodide*, prepared in acetone, sintered at 167—169° but was not completely melted at 200° (Found: C, 38·3; H, 6·4; N, 4·8; I, 45·2. $C_9H_{18}ONI$ requires C, 38·2; H, 6·4; N, 4·9; I, 44·9%). A small quantity, crystallised rapidly, separated unchanged from methanol as needles, but longer boiling led to decomposition with separation of trimethylammonium iodide, m. p. > 260° (Found: C, 20·8; H, 5·6; I, 67·2. Calc. for $C_3H_{10}NI$: C, 19·3; H, 5·4; I, 67·9%).

2-*Dimethylaminomethyl*cyclo*heptanone*, prepared similarly from *cyclo*heptanone, had b. p. 122—124°/16 mm., n_D^{21} 1·4700 (Found: C, 70·9; H, 11·0; N, 8·2. $C_{10}H_{19}ON$ requires C, 71·0; H, 11·2; N, 8·3%). The *methiodide*, prepared in acetone, separated only on addition of ether. After crystallisation from a little ethanol it formed prisms, m. p. 129—130° (decomp.) (Found: C, 42·4; H, 6·4; N, 4·6; I, 41·0. $C_{11}H_{22}ONI$ requires C, 42·1; H, 7·1; N, 4·5; I, 40·8%).

α*α*′-*Bisdimethylaminomethyl*cyclo*alkanones*.—A mixture of *cyclo*hexanone (98 g.), dimethylamine hydrochloride (163 g.), and 37% aqueous formaldehyde (167 g.) was heated under reflux on the steam-bath with rapid stirring. A vigorous exothermic reaction took place (occasionally this required initiation by a few drops of concentrated hydrochloric acid). After being heated for a further ½ hr. the mixture was evaporated to dryness *in vacuo*. The residual solid was washed with hot ethanol and dried, to give 2 : 6-*bis*(*dimethylaminomethyl*)cyclo*hexanone dihydrochloride* (IX*e*) (200 g.), m. p. 165—166° raised to 169—170° on crystallisation from 95% aqueous ethanol (Found: C, 50·4; H, 9·0; N, 10·1; Cl, 24·9. $C_{12}H_{26}ON_2Cl_2$ requires C, 50·5; H, 9·1; N, 9·8; Cl, 24·9%). The *base* liberated with the theoretical quantity of sodium hydroxide and isolated in the usual way had b. p. 90—94°/0·4 mm. (Found: C, 67·6; H, 11·0; N, 13·4. $C_{12}H_{24}ON_2$ requires C, 67·9; H, 11·3; N, 13·2%). The *dioxalate*, prepared in ethanol, had m. p. 134° (Found: C, 48·4; H, 7·1; N, 6·9. $C_{16}H_{28}O_9N_2$ requires C, 48·8; H, 7·2; N, 7·2%). The *dimethiodide*, prepared in methanol, separated as needles, which sintered at 208—210° but were not completely melted at 240° (Found: C, 33·8; H, 6·2; N, 5·7; I, 51·4. $C_{14}H_{30}ON_2I_2$ requires C, 33·9; H, 6·1; N, 5·6; I, 51·3%).

2 : 5-*Bisdimethylaminomethyl*cyclo*pentanone dihydrochloride* (as IX*d*), similarly prepared, had m. p. 185—186° (from methanol) (Found: C, 48·4; H, 9·0; N, 10·0; Cl, 26·0. $C_{11}H_{24}ON_2Cl_2$ requires C, 48·7; H, 8·9; N, 10·3; Cl, 26·2%). The *base*, crystallised from light petroleum (b. p. 40—60°), had m. p. 44° (Found: C, 66·8; H, 11·2; N, 14·1. $C_{11}H_{22}ON_2$ requires C, 66·7; H, 11·1; N, 14·2%). The hygroscopic *dioxalate* (from ethanol–ether) had m. p. 120° (Found: C, 46·8; H, 6·9; N, 7·3. $C_{15}H_{26}O_9N_2$ requires C, 47·6; H, 6·9; N, 7·4%). The *dimethiodide* separated in granules from acetone and sintered above 155° (Found: C, 31·1; H, 5·9; N, 5·8; I, 52·6. $C_{13}H_{28}ON_2I_2$ requires C, 32·4; H, 5·8; N, 5·8; I, 52·7%); in boiling methanol it rapidly decomposed.

2 : 7-*Bisdimethylaminomethyl*cyclo*heptanone dihydrochloride* (as IX*f*), similarly prepared, had m. p. 170—171° (from ethanol) (Found: C, 52·7; H, 8·4; N, 9·3; Cl, 23·7. $C_{13}H_{28}ON_2Cl_2$ requires C, 52·2; H, 9·4; N, 9·4; Cl, 23·8%). The *base*, liberated at 0° with the theoretical quantity of sodium hydroxide, had b. p. 100—104°/0·5 mm. (Found: C, 68·3; H, 10·9; N, 12·5. $C_{13}H_{26}ON_2$ requires C, 69·0; H, 11·5; N, 12·4%). The *dioxalate*, prepared in ethanol and

[11] Frank and Pierle, *J. Amer. Chem. Soc.*, 1951, **73**, 724.

crystallised from methanol, formed needles, m. p. 140—141° (Found: C, 50·8; H, 7·3; N, 7·1. $C_{17}H_{30}O_9N_2$ requires C, 50·3; H, 7·4; N, 6·9%). The *dimethiodide*, prepared in acetone and crystallised from methanol, gave needles, m. p. 210—212° (decomp. from 180°) (Found: C, 35·4; H, 6·2; N, 5·4; I, 49·3. $C_{15}H_{32}ON_2I_2$ requires C, 35·3; H, 6·3; N, 5·5; I, 49·8%).

2-Pyridyl-alcohols (I) *and* (V).—The alcohols listed in Table 1 were prepared from 2-pyridyllithium and the corresponding ketone as described in Part III.[12]

3-Acetyl-1-methylpyrrocoline.—(i) 1-Piperidino-3-2′-pyridylbutan-1-ol (I*a*) (177 g.), b. p. 120—130°/0·5 mm., and acetic anhydride (1770 ml.) were boiled under reflux for 24 hr. After removal of excess of anhydride, the product was poured into water. The precipitated solid was filtered off, washed, dried, and distilled. The fraction (59 g.) having b. p. 140—150°/3·5 mm. recrystallised from light petroleum (b. p. 60—80°) (600 ml.), to give 3-acetyl-1-methylpyrrocoline (II*a*) (52 g., 40%), large yellow prisms, m. p. 100—101°.

(ii) The butanol (I*a*) (148 g.) and acetic anhydride (1480 ml.) were boiled under reflux for 6 hr. and worked up as in (i), to give the pyrrocoline (II*a*) (12 g.). The aqueous filtrate on basification and extraction gave an oil (96 g.) which was distilled, to give *1-piperidino-3-2′-pyridylbutyl acetate* (82 g.), b. p. 140—150°/0·5 mm. (Found: C, 69·5; H, 8·8; N, 10·1; Ac, 14·9. $C_{16}H_{24}O_2N_2$ requires C, 69·3; H, 8·7; N, 10·1; Ac, 15·1%). The *oxalate* (from ethanol) had m. p. 169—170° (decomp.) (Found: C, 58·9; H, 7·4; N, 7·5; Ac, 11·6. $C_{16}H_{26}O_6N_2$ requires C, 59·0; H, 7·1; N, 7·7; Ac, 11·7%). The acetate (80 g.) was re-boiled with acetic anhydride (800 ml.) for 6 hr. and worked up, to give the pyrrocoline (II*a*) (18 g.) and recovered acetate (45 g.). The latter, after a third treatment with acetic anhydride for 18 hr. gave pyrrocoline (II*a*) (13 g.). The total yield of acetylpyrrocoline (II*a*), m. p. 98—100°, was 43 g.

(iii) A sample of the butanol (I*a*) (120 g.), having a boiling range 125—170°/0·5 mm., when cyclised and worked up as in (i) gave crude solid (21·5 g.) from which, in addition to acetylpyrrocoline (II*a*), there was isolated by fractional crystallisation from light petroleum (b. p. 40—60°) the less soluble *2-acetoxymethyl-3-acetyl-1-methylpyrrocoline* (II; R^1 = Me, R^2 = CH_2·OAc) as fawn needles, m. p. 97° depressed on admixture with acetylpyrrocoline (II*a*) to 68—71° (Found: C, 69·1; H, 6·4; N, 5·8; Ac, 35·8. $C_{14}H_{15}O_3N$ requires C, 68·6; H, 6·1; N, 5·7; Ac, 35·2%), $\lambda_{max.}$ 230, 261, 267, and 378 mμ (ε 19,000, 14,000, 14,000, and 13,000).

3-Acetyl-1 : 2-dialkylpyrrocolines.—1-Dimethylamino-2-methyl-3-2′-pyridylpentan-3-ol (I*b*) (55 g.) and acetic anhydride (550 ml.) were boiled under reflux for 24 hr. After removal of excess of anhydride, the product was poured into water and extracted with ether. The ether layer was filtered (charcoal and kieselguhr) and evaporated. On addition of water the crude pyrrocoline solidified and was filtered off, washed, dried in the air, and distilled. The fraction having b. p. 140—148°/0·1 mm. solidified and after crystallisation from light petroleum (b. p. 60—80°) gave *3-acetyl-1-ethyl-2-methylpyrrocoline* (II*b*) (27 g.), lemon-yellow prisms, m. p. 82°.

The *alkylpyrrocolines* (II*c–e*) (Table 2) were prepared similarly.

1-Alkylpyrrocolines.—3-Acetyl-1-methylpyrrocoline (5 g.) in concentrated hydrochloric acid (30 ml.) was boiled till the initial orange colour disappeared (*ca.* 2 min.). The mixture was cooled and basified with ammonia. The solid was filtered off, washed, dried, and sublimed at 70—80°/0·5 mm., to give *1-methylpyrrocoline* (III*a*) (3·5 g.), cream-coloured, m. p. 44° (Found: C, 82·4; H, 6·7; N, 11·0. C_9H_9N requires C, 82·4; H, 6·9; N, 10·7%), $\lambda_{max.}$ 240, 280, 288, 300, and 360 mμ (ε 33,000, 2100, 3200, 4400, 2000 in EtOH). 1 : 2-Dimethylpyrrocoline (III*d*), similarly prepared, had m. p. 61—62° (Holland and Naylor [2] give m. p. 63°), $\lambda_{max.}$ 243, 284, 294, 305, 360 mμ (ε 28,000, 1800, 2350, 2700, 1900).

Pyrrocolines (III*b*), (III*c*), and (III*e*) formed pale yellow fluorescent oils. All had the strong naphthalene-like smell characteristic of alkylpyrrocolines, and decomposed rapidly in air.

3-Acetyl-1-2′-(tertiary amino)alkylpyrrocolines.—1 : 5-Bis(dimethyl amino)-2 : 4-dimethyl-3-2′-pyridylpentan-3-ol (V*b*) (69 g.) and acetic anhydride (700 ml.) were boiled under reflux for 24 hr. After removal of excess of anhydride the product was poured into water and extracted with ether. The ether layer was discarded. The aqueous layer was basified by 5N-sodium hydroxide and extracted with ether. After removal of the ether the oil was distilled. The fraction (25 g.) having b. p. 160—164°/0·5 mm. solidified and after crystallisation from light petroleum (b. p. 40—60°) gave *3-acetyl-1-(2-dimethylamino-1-methylethyl)-2-methylpyrrocoline* (VI*b*) (18 g.) as pale yellow prisms, m. p. 72°. The colourless *oxalate* (from ethanol) had m. p. 178°. The colourless *methiodide*, prepared in acetone, had m. p. 201° (Found: C, 50·9; H, 6·5; N, 6·9; I, 32·1. $C_{17}H_{25}ON_2I$ requires C, 51·0; H, 6·25; N, 7·0; I, 31·8%).

[12] Adamson and Billinghurst, *J.*, 1950, 1039.

The *aminoalkylpyrrocolines* (VI*a*, *c*, and *d*) (Table 2) were prepared similarly.

1-(2-*Dimethylamino*-1-*methylethyl*)-2-*methylpyrrocoline*.—The acetylpyrrocoline (11 g.) and concentrated hydrochloric acid (50 ml.) were boiled till the initial deep yellow colour disappeared (*ca.* 2 min.). The mixture was cooled, basified with ammonia, and extracted with ether, and the ether evaporated to give the pyrrocoline (VII*b*) as a yellow oil, $\lambda_{max.}$ 243, 280, 290, 301, and 350 mμ (ε 29,600, 2000, 2700, 3000, 2300). The colourless *oxalate*, prepared in ethanol–ether, had m. p. 138—140° (Found: C, 62·5; H, 7·1; N, 9·4. $C_{14}H_{22}O_4N_2$ requires C, 62·8; H, 7·2; N, 9·2%). The *methiodide*, prepared in ethanol–ether, had m. p. 177° (Found: C, 50·3; H, 6·2; I, 35·4. $C_{15}H_{23}N_2I$ requires C, 50·3; H, 6·4; I, 35·5%).

Attempted Preparation of 2-(*Tertiary amino*)*methylpyrrocolines*.—When the amino-2-pyridylalkanols (I*f*) and (I*g*) were submitted to cyclisation as described above, no pyrrocoline derivative could be detected in the products by ultraviolet spectroscopy.

4-*Acetyl*-2 : 3-*dihydro*-1H-cyclo*penta*[a]*pyrrocoline* (XIV*a*).—2-Dimethylaminomethylcyclopentanone (58 g.) was treated with 2-pyridyl-lithium as described in Part III,[12] to give mixed isomers of 2-*dimethylaminomethyl*-1-2′-*pyridyl*cyclo*pentanol* (X*a*) (46 g.), b. p. 112—118°/0·2 mm. (Found: C, 72·0; H, 9·0; N, 12·0. $C_{13}H_{20}ON_2$ requires C, 70·9; H, 9·1; N, 12·7%). The *cyclo*pentanol and acetic anhydride (460 ml.) were boiled for 6 hr. After removal of excess of anhydride the product was poured into water and extracted with ether. The ether layer was washed with 0·5N-hydrochloric acid (2 × 75 ml.) and evaporated. The residue, on crystallisation from light petroleum (b. p. 40—60°), gave the cyclo*penta*[a]*pyrrocoline* (XIV*a*) (0·9 g.) as straw-coloured prisms, m. p. 109—110° (Found: C, 78·5; H, 6·6; N, 7·4. $C_{13}H_{13}ON$ requires C, 78·5; H, 6·6; N, 7·1%), $\lambda_{max.}$ 230, 256, 275, 371, and 383 mμ (ε 21,500, 12,200, 25,700, 13,600, and 12,200). The aqueous filtrate and acid washings were combined and basified. The oil was extracted with ether, and the ether evaporated. The residue (27 g.) and acetic anhydride were boiled for 6 hr. On working up as above, no further pyrrocoline was isolated. The basic oil (22 g.) (Found: Ac, 4·3%) was hydrolysed by boiling with 2N-hydrochloric acid (100 ml.) for 2 hr., and on working up gave the *trans*-alcohol (X*a*) (19 g.), b. p. 108—110°/0·4 mm. (Found: C, 71·0; H, 9·0; N, 11·5%). The *trans*-alcohol (19 g.) was heated in concentrated sulphuric acid (190 ml.) on the steam-bath for ½ hr. After pouring on ice and working up in the usual way there was obtained a mixture of 2-dimethylaminomethyl-1- (XII*a*) and 3-dimethylamino-2-2′-pyridyl*cyclo*pentene (XIII*a*) (15 g.) (Found: C, 76·7; H, 8·9; N, 13·7. Calc. for $C_{13}H_{18}N_2$: C, 77·2; H, 9·0; N, 13·9), $\lambda_{max.}$ 250 and 284 (ε 9500 and 6800). Cyclisation by the method described in Part VII [1] afforded the pyrrocoline (XIV*a*) (1·5 g.), m. p. and mixed m. p. 109—110°, and recovered *cyclo*pentene (XIII*a*), (9 g.) b. p. 98—108°/0·5 mm. (Found: C, 77·0; H, 8·7%).

6-*Acetyl*-7 : 8 : 9 : 10-*tetrahydrobenzo*[a]*pyrrocoline* (XIV*b*).—(i) 2-Dimethylaminomethylcyclohexanone (39 g.) with 2-pyridyl-lithium gave mixed isomers of 2-*dimethylaminomethyl*-1-2′-*pyridyl*cyclo*hexanol* (X*b*) (42 g.), b. p. 140—144°/2·5 mm. (Found: C, 71·9; H, 9·3; N, 11·5. $C_{14}H_{22}ON_2$ requires C, 71·8; H, 9·4; N, 12·0%), $\lambda_{max.}$ 260 mμ (ε 3400). The *oxalate* (from ethanol) had m. p. 174—176° (Found: C, 59·5; H, 7·4; N, 8·5. $C_{14}H_{22}ON_2,C_2H_2O_4$ requires C, 59·3; H, 7·4; N, 8·7%). The hexanol (X*b*) (50 g.) and acetic anhydride (500 ml.) were boiled for 6 hr. Working up as described above gave a non-basic solid (4·0 g.) which on crystallisation from light petroleum (b. p. 60—80°) gave 6-*acetyl*-7 : 8 : 9 : 10-*tetrahydrobenzo*[a]*pyrrocoline* (XIV*b*) (1·2 g.), yellow prisms, m. p. 117° (Found: C, 78·8; H, 6·9; N, 6·5. $C_{14}H_{15}ON$ requires C, 78·9; H, 7·1; N, 6·6%), $\lambda_{max.}$ 230, 276 and 370 mμ (ε 19,000, 21,000, and 13,000). The filtrate and washings afforded a basic oil (49 g.), which was boiled for a further 6 hr. with acetic anhydride (500 ml.). Working up gave the pyrrocoline (XIV*b*) (0·4 g.) and a basic oil (46 g.). The oil was boiled for a third period of 6 hr. with acetic anhydride. Working up gave a basic oil (42 g.), but no isolable pyrrocoline. The oil, when distilled, gave trans-2-*dimethylaminomethyl*-1-2′-*pyridyl*cyclo*hexyl acetate* (XI*b*) (38 g.), b. p. 136—138°/0·5 mm. (Found: C, 69·7; H, 8·7; N, 9·5; Ac, 15·0. $C_{16}H_{24}O_2N_2$ requires C, 69·6; H, 8·7; N, 10·1; Ac, 15·6%). The acetate was hydrolysed for 2 hr. with boiling 2N-hydrochloric acid (200 ml.). The recovered *trans*-alcohol (31 g.) on dehydration gave mixed *cyclo*alkenes (XII*b*) and (XIII*b*) (19 g.) [$\lambda_{max.}$ 242, 276 mμ (ε 7800, 5000)], which were separated and behaved on cyclisation as described below.

(ii) Mixed isomeric hexanols (X*b*) (40 g.) were dehydrated in concentrated sulphuric acid (200 ml.) on the steam-bath for ½ hr., affording an oil (29 g.), which partially solidified. The solid (10 g.) was filtered off and crystallised from light petroleum (b. p. 40—60°), to give

3-*dimethylaminomethyl*-2-2′-*pyridyl*cyclo*hexene* (XIII*b*), m. p. 43—45° (Found: C, 77·7; H, 9·2; N, 12·9. $C_{14}H_{20}N_2$ requires C, 77·8; H, 9·3; N, 13·0%), $\lambda_{max.}$ 243 and 280 mμ (ε 9000 and 7800); the *oxalate* (from ethanol) had m. p. 190—191° (Found: C, 62·9; H, 7·2; N, 8·7. $C_{16}H_{22}O_4N_2$ requires C, 62·8; H, 7·2; N, 9·2%). The oily filtrate (19 g.) was converted into its oxalate in ethanol (200 ml.) and next morning the oxalate of (XIII*b*) (12·8 g.) was filtered off (m. p. and mixed m. p. 189—191°). On basification it gave the base (8·2 g.), m. p. and mixed m. p. 42—44°. The filtrate from the oxalate preparation was evaporated to dryness, and the residue converted into a base, which was distilled to give an oil (9·0 g.), b. p. 108—114°/0·1 mm., substantially 2-dimethylaminomethyl-1-2′-pyridyl*cyclo*hexene (XII*b*), $\lambda_{max.}$ 242 and 280 mμ (ε 8500 and 7500). On cyclisation by the usual method it gave acetylpyrrocoline (XIV*b*) (2·4 g.), m. p. and mixed m. p. 116—117°. The *cyclo*hexene (XIII*b*) (42 g.), submitted to the usual cyclisation procedure,[1] was recovered unchanged (38 g.; m. p. and mixed m. p. 42—44°).

6-*Acetyl*-8 : 9 : 10 : 11-*tetrahydro*-7-cyclo*hepta*[a]*pyrrocoline* (XIV*c*).—(i) 2-Dimethylaminomethyl*cyclo*heptanone (85 g.) with 2-pyridyl-lithium gave 2-*dimethylaminomethyl*-1-2′-*pyridyl*cyclo*heptanol* (X*c*) (117 g.), b. p. 140—143°/0·4 mm. (Found: C, 72·4; H, 9·4; N, 11·5. $C_{15}H_{24}ON_2$ requires C, 72·6; H, 9·7; N, 11·3%). The *oxalate* (from ethanol) had m. p. 162—164° (Found: C, 60·3; H, 7·8; N, 7·8. $C_{17}H_{26}O_5N_2$ requires C, 60·4; H, 7·7; N, 8·3%). The *methiodide*, prepared in acetone and crystallised from methanol, had m. p. 210—211° (decomp.) (Found: C, 49·2; H, 7·0; N, 7·0; I, 32·4. $C_{16}H_{27}ON_2I$ requires C, 49·2; H, 7·0; N, 7·2; I, 32·6%). The *cyclo*heptanol (50 g.) was cyclised as described above for the *cyclo*pentanol (X*a*) to give (i) a non-basic oil (2·5 g.), substantially the acetylpyrrocoline (XIV*c*), $\lambda_{max.}$ 232, 268, 276, and 374 mμ (ε 16,000, 13,000, 14,000, and 7000), from which the pure compound was not isolated, and (ii) a basic oil which was distilled (b. p. 140—150°/0·6 mm.) (36 g.) and recrystallised from light petroleum (b. p. 40—60°) to give trans-2-*dimethylaminomethyl*-1-2′-*pyridyl*cyclo*heptyl acetate* (XI*c*) (17 g.), m. p. 52—54° (Found: C, 70·2; H, 8·8; N, 9·5; Ac, 15·1. $C_{17}H_{26}O_2N_2$ requires C, 70·4; H, 8·9; N, 9·6; Ac, 14·8%). (ii) The *cyclo*heptanol (X*c*) (19 g.) was dehydrated in concentrated sulphuric acid at 100° for ½ hr. Working up gave substantially the mixed (or a pure) *cyclo*heptenes (XII*c* and/or XIII*c*) (7 g.), $\lambda_{max.}$ 244 and 277 mμ (ε 9400 and 7500). On cyclisation no pyrrocoline was isolated.

7 : 8 : 9 : 10-*Tetrahydrobenzo*[a]*pyrrocoline*.—The acetylpyrrocoline (XIV*b*) was hydrolysed as described above, and the crude product sublimed *in vacuo* to give the colourless *pyrrocoline* (XV*b*), m. p. 59—60° depressed on admixture with the parent acetyl compound to 42—45° (Found: C, 84·4; H, 7·4; N, 8·4. $C_{12}H_{13}N$ requires C, 84·2; H, 7·6; N, 8·2%), $\lambda_{max.}$ 244, 250, 287, 296, 308, and 360 mμ (ε 29,000. 30,000, 2300, 3000, 4200, 2100).

4-*Acetyl*-1-*dimethylaminomethyl*-2 : 3-*dihydro*-1H-cyclo*penta*[a]*pyrrocoline* (XIV*d*).—The diamino-ketone (IX*d*) (44 g.) was treated with 2-pyridyl-lithium to give 2 : 5-*bisdimethylaminomethyl*-1-2′-*pyridyl*cyclo*pentanol* (31 g.), b. p. 135—137°/0·5 mm. (Found: C, 69·6; H, 9·5; N, 14·7. $C_{16}H_{27}ON_3$ requires C, 69·4; H, 9·8; N, 15·2%). This (30 g.) was cyclised as described above. After removal of excess of anhydride the product was poured into water. The aqueous layer was decanted from tar and basified, and the oil isolated with ether and extracted with boiling light petroleum (b. p. 40—60°). The light petroleum extracts were evaporated to give an oil (3·5 g.) shown by light absorption [$\lambda_{max.}$ 230, 270, and 370 mμ (ε 5400, 5500, and 1200)] to contain *ca.* 10% of acetyl-pyrrocoline, probably (XIV*d*).

6-*Acetyl*-10-*dimethylaminomethyl*-7 : 8 : 9 : 10-*tetrahydrobenzo*[a]*pyrrocoline* (XIV*e*)—(i) 2 : 6-Bisdimethylaminomethyl*cyclo*hexanone (80 g.) with 2-pyridyl-lithium gave mixed isomers of 2 : 6-*bisdimethylaminomethyl*-1-2′-*pyridyl*cyclo*hexanol* (X*e*) (55 g.), b. p. 140—155°/0·5 mm. (Found: C, 70·1; H, 9·8; N, 14·1. $C_{17}H_{29}ON_3$ requires C, 70·1; H, 10·0; N, 14·4%). This (52 g.) was boiled with acetic anhydride (500 ml.) for 6 hr. After removal of excess of anhydride the product was poured into water. The solution was filtered (charcoal) from tar and basified. The liberated oil (26 g.) was isolated with ether and distilled, three fractions being collected: (i) 150—160°/0·5 mm. (11 g.), (ii) 160—190°/0·5 mm. (8 g.), and (iii) 190—195°/0·5 mm. (3·9 g.). The orange, viscous fraction (iii) solidified after several days and crystallised from light petroleum (b. p. 40—60°), to give 6-*acetyl*-10-*dimethylaminomethyl*-7 : 8 : 9 : 10-*tetrahydrobenzo*[a]*pyrrocoline* (XIV*e*) (1·7 g.) as cream-coloured crystals, m. p. 70—71° (Found: C, 75·2; H, 8·3; N, 10·6. $C_{17}H_{22}ON_2$ requires C, 75·5; H, 8·2; N, 10·4%), $\lambda_{max.}$ 230, 275, 370, and 382 mμ (ε 19,000, 20,000, 11,500, and 10,400). The sparingly soluble *oxalate* separated as a gel from cold ethanol, but became crystalline on boiling. It had m. p. 240—241° (Found: C, 63·3; H, 6·6; N, 7·7. $C_{19}H_{24}O_5N_2$ requires C, 63·4; H, 6·7; N, 7·8%). The cream-coloured

methiodide, prepared in acetone and crystallised from methanol, had m. p. 265° (decomp.) (Found: C, 52·7; H, 6·2; N, 6·7; I, 31·0. $C_{18}H_{25}ON_2I$ requires C, 52·4; H, 6·1; N, 6·8; I, 30·8%), $\lambda_{max.}$ 229, 272, and 363 mμ (ε 31,000, 24,000, and 12,600). Fraction (i) solidified and, crystallised from light petroleum (b. p. 40—60°), gave trans-trans-2 : 6-*bisdimethylaminomethyl*-1-2′-*pyridyl*cyclo*hexyl acetate* (XI*e*) (4·2 g.), prisms, m. p. 76—78° (Found: C, 68·8; H, 9·2; N, 12·3; Ac, 14·8. $C_{19}H_{31}O_2N_3$ requires C, 68·5; H, 9·3; N, 12·6; Ac, 12·9%). The colourless *dioxalate* (from ethanol) had m. p. 185—186° (Found: C, 52·8; H, 7·2; N, 7·7. $C_{23}H_{35}O_{10}N_3$ requires C, 53·8; H, 6·8; N, 8·2%). The residues from the crystallisation of fraction (i) were combined with fraction (ii) and converted into the oxalate in ethanol. The precipitated mixed oxalates of the pyrrocoline (XIV*e*) and *cyclo*hexyl acetate (XI*e*) were filtered off. The filtrate was evaporated and the residue dissolved in water, basified, and extracted three times with ether. The ether was evaporated to an oil which was distilled. The fraction having b. p. 150—165°/0·2 mm. solidified after several days and, crystallised from light petroleum (b. p. 60—80°), gave trans-trans-2-*acetoxymethyl*-6-*dimethylaminomethyl*-1-2′-*pyridyl*-cyclo*hexyl acetate* (XI*g*) (2·3 g.), prisms, m. p. 100° (Found: C, 65·6; H, 8·3; N, 8·0; Ac, 24·2. $C_{19}H_{28}O_4N_2$ requires C, 65·6; H, 8·0; N, 8·0; Ac, 24·8%).

(ii) The *cyclo*hexanol (X*e*) (59 g.) was heated in acetic anhydride (500 ml.) till just boiling, and the excess of anhydride then immediately removed *in vacuo*. The residue was poured into water and cautiously basified with ammonia. The liberated oil (59 g.) was isolated by 3 extractions with ether and substantially solidified. Recrystallisation from light petroleum (b. p. 40—60°) gave the *trans-trans*-acetate (XI*e*) (40 g.), m. p. and mixed m. p. 76—78°. The residual mixed isomeric acetates (21 g.) on cyclisation behaved as described under (i).

(iii) The *trans-trans-cyclo*hexyl acetate (XI*e*) (20 g.), submitted to cyclisation, was substantially recovered unchanged (15 g.); m. p. and mixed m. p. 183—185°. There was also isolated the diacetate (XI*g*) (1·3 g.), m. p. and mixed m. p. 99—100°.

6-*Acetyl*-11-*dimethylaminomethyl*-8 : 9 : 10 : 11-*tetrahydro*-7H-cyclo*hepta*[a]*pyrrocoline* (XIV*f*).—(i) *Cyclisation of the mixed* cyclo*heptanols* (X*f*). 2 : 7-Bisdimethylaminomethyl-*cyclo*heptanone (IX*f*) (68 g.) with 2-pyridyl-lithium gave mixed isomers of 2 : 7-*bisdimethylaminomethyl*-1-2′-*pyridyl*cyclo*heptanol* (X*f*) (42 g.), b. p. 152—156°/0·4 mm. (Found: C, 71·2; H, 10·3; N, 13·7. $C_{18}H_{31}ON_3$ requires C, 70·8; H, 10·2; N, 13·8%). This material was boiled with acetic anhydride (420 ml.) for 6 hr. The excess of anhydride was removed and the residue dissolved in water, basified with ammonia, and extracted with ether,[6] tar being filtered off. The ether was evaporated to an oil (36 g.), which was freed from resin by dissolution in hot light petroleum (b. p. 40—60°). The light petroleum extracts were evaporated to an oil (30 g.) which was converted into the oxalate in ethanol. The precipitated oxalate was filtered off, washed, dried (13 g.; m. p. 210°), and crystallised from methanol, to give 6-*acetyl*-11-*dimethylaminomethyl*-8 : 9 : 10 : 11-*tetrahydro*-7H-cyclo*hepta*[a]*pyrrocoline oxalate* (cf. XIV*f*) (10 g.) as fawn-coloured needles, m. p. 210° (Found: C, 64·3; H, 7·0; N, 7·5. $C_{18}H_{24}ON_2,C_2H_2O_4$ requires C, 64·2; H, 7·0; N, 7·5%), $\lambda_{max.}$ 230, 272, and 366 mμ (ε 27,000, 21,000, and 11,500). The base formed an amber oil. The *methiodide*, prepared in acetone and crystallised from ethanol, formed almost colourless prisms, m. p. 242—244° (decomp.) (Found: C, 53·6; H, 6·9; N, 6·0; I, 27·2; loss at 100° *in vacuo*, 8·7. $C_{19}H_{27}ON_2I,C_2H_5{\cdot}OH$ requires C, 53·4; H, 7·0; N, 5·9; I, 27·0; loss, 9·7. Found, on a dried sample: C, 54·1; H, 6·3; N, 6·6; I, 29·7. $C_{19}H_{27}ON_2I$ requires C, 53·5; H, 6·4; N, 6·6; I, 29·8%), $\lambda_{max.}$ 232, 262, and 366 mμ (ε 31,000, 21,000, and 11,000). The filtrate from the oxalate preparation was evaporated. To the residue water and ether were added and the whole was basified by aqueous ammonia. The ether was evaporated and the residual oil (16 g.) was distilled. The fraction having b. p. 190—210°/0·5 mm. (10 g.) was dissolved in ether and washed several times with N-hydrochloric acid. The residue (5 g.) left on evaporation of the ether layer was recrystallised several times from light petroleum (b. p. 60—80°), to give 11-*acetoxymethyl*-6-*acetyl*-8 : 9 : 10 : 11-*tetrahydro*-7H-cyclo*hepta*[a]*pyrrocoline* (XIV*h*) (3·7 g.), pale yellow prisms or needles, m. p. 112° (Found: C, 72·2; H, 6·9; N, 4·6; Ac, 29·0. $C_{18}H_{21}O_3N$ requires C, 72·3; H, 7·0; N, 4·7; Ac, 28·8%), $\lambda_{max.}$ 231, 274, 368, and 383 (infl.) (ε 26,000, 23,000, 13,000, and 11,600).

(ii) *Separation of* cis-trans- *and* trans-trans-cyclo*heptanols* (X*f*) via *the* cyclo*heptyl acetate oxalates* (XI*f*). A second preparation of mixed *cyclo*heptanols (X*f*) (133 g.) (b. p. 160—170°/0·5 mm.) substantially solidified and, recrystallised from light petroleum (b. p. 40—60°) at *ca.* −20°, gave a solid mixture (A) of *cis-trans-* and *trans-trans-cyclo*heptanol (X*f*) (74 g.), m. p. 45—55°, and non-crystallisable residues (B; 62 g.). The solid (A) was heated in acetic anhydride (300

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ml.) till just boiling, the excess of anhydride immediately removed *in vacuo*, and the acetate isolated by basification and ether-extraction (four times). The mixed acetates were converted into the oxalate in ethanol with anhydrous oxalic acid (50 g.), precipitation being initiated by addition of a little ether. After 4 hr., the oxalate was filtered off (filtrate C), washed with ethanol and ether (40 g.; m. p. 180—185°), and recrystallised from methanol, to give cis-trans-2 : 7-bisdimethylaminomethyl-1-2′-pyridyl*cyclo*hexyl acetate oxalate (as XI*f*) (32 g.), prisms, m. p. 195—196°. It was dissolved in a little water and basified. The solid base was filtered off, washed, dried, and crystallised from light petroleum (b. p. 40—60°) to give cis-trans-2 : 7-*bisdimethylaminomethyl*-1-2′-*pyridyl*cyclo*heptyl acetate* (XI*f*) (18 g.), m. p. 87—89°, depressed to 56—62° on admixture with the *trans-trans*-isomer described below (Found: C, 69·7; H, 9·7; N, 12·1; Ac, 12·5. $C_{20}H_{33}O_2N_3$ requires C, 69·2; H, 9·5; N, 12·1; Ac, 12·4%). Hydrolysis with 2N-hydrochloric acid on the steam-bath for 2 hr. and crystallisation of the crude product from light petroleum (b. p. 40—60°) gave cis-trans-2 : 7-*bisdimethylaminomethyl*-1-2′-*pyridyl*-cyclo*heptanol* (X*f*), m. p. 84—86°, depressed to 58—61° on admixture with the *trans-trans*-isomer described below (Found: C, 70·8; H, 9·6; N, 14·0. $C_{18}H_{31}ON_3$ requires C, 70·8; H, 10·2; N, 13·8%).

The filtrate C was evaporated and the residue converted into a base, which slowly solidified and, recrystallised from light petroleum (b. p. 40—60°) at *ca.* −20°, gave trans-trans-2 : 7-*bisdimethylaminomethyl*-1-2′-*pyridyl*cyclo*heptyl acetate* (XI*f*) (25 g.), m. p. 86°, depressed to 53—60° on admixture with the *cis-trans*-isomer (Found: C, 68·7; H, 9·3; N, 11·4; Ac, 13·0%). The oxalate separated from a small volume of ethanol only on addition of ether. It was difficult to recrystallise and was not obtained pure. The *trans-trans*-acetate (XI*f*) (2 g.) and 2N-hydrochloric acid (20 ml.) were heated on the steam-bath for 2 hr., cooled, and basified. The oil solidified and was filtered off, washed, dried, and recrystallised from light petroleum (b. p. 40—60°) at *ca.* −20°, to give trans-trans-2 : 7-*bisdimethylaminomethyl*-1-2′-*pyridyl*cyclo*heptanol* (X*f*), m. p. 82°, depressed to 56—61° on admixture with the *cis-trans*-heptanol described above (Found: C, 70·6; H, 10·0; N, 14·0. $C_{18}H_{31}ON_3$ requires C, 70·8; H, 10·2; N, 13·8%). The non-crystallisable residue (B) (62 g.), acetylated and separated as described above, gave *cis-trans*-acetate oxalate (as XI*f*) (10 g.), m. p. 194°, and *trans-trans*-acetate (XI*f*), m. p. and mixed m. p. 86—87°.

An earlier preparation of mixed *cyclo*heptanols (X*f*) (b. p. 155—160°/0·5 mm.) (149 g.) partially solidified during several days and crystallised at *ca.* −20° from light petroleum (b. p. 40—60°) (300 ml.); washing with cold solvent gave the pure *cis-trans-cyclo*heptanol (X*f*) (60 g.), m. p. 82°, not depressed on admixture with the sample described above. In all subsequent preparations the solid *cyclo*heptanol proved to be a mixture of the *cis-trans-* and *trans-trans*-forms as described above.

(iii) *Cyclisation of the* cis-trans-*acetate* (XI*f*). The acetate (14 g.) and acetic anhydride (150 ml.) were boiled for 6 hr. Working up as described under (i) gave acetylpyrrocoline oxalate (cf. XIV*f*) (8 g.), m. p. and mixed m. p. 209°, a non-basic oil (3·8 g.) which partially solidified when seeded with acetoxymethylpyrrocoline (XIV*h*), and a basic oil (2 g.) which did not solidify when seeded with either of the isomeric acetates (XI*f*).

(iv) *Cyclisation of the* trans-trans-*acetate* (XI*f*). The acetate (20 g.) and acetic anhydride (200 ml.) were boiled for 6 hr. After removal of excess of anhydride the product was poured into water, basified and extracted three times with ether. The ether extracts on evaporation gave solid (15 g.) which was distilled. The fraction having b. p. 150—160°/0·5 mm. (11 g.) crystallised from light petroleum (b. p. 40—60°), to give recovered *trans-trans*-acetate (XI*f*) (9·2 g.), m. p. and mixed m. p. 86—87°. The residue in the distillation flask gave no solid oxalate when treated in ethanol with oxalic acid.

11-*Dimethylaminomethyl*-8 : 9 : 10 : 11-*tetrahydro*-7H-cyclo*hepta*[a]*pyrrocoline* (XV*f*).—The acetyl compound (XIV*f*) was hydrolysed as described above, and the crude product sublimed at 130°/0·5 mm., to give the colourless *pyrrocoline* (XV*f*), m. p. 82—83°. The compound also crystallised well from light petroleum (b. p. 40—60°) as large colourless prisms (Found: C, 79·2; H, 9·0; N, 11·5. $C_{16}H_{22}N_2$ requires C, 79·4; H, 9·1; N, 11·6%), $\lambda_{max.}$ 243, 283, 292, 303, and 360 mμ (ε 31,000, 2000, 2500, 2800, and 2300). The almost colourless *oxalate*, crystallised from ethanol, had m. p. 175—178° (decomp.) (Found: C, 64·4; H, 7·3; N, 8·2. $C_{18}H_{24}O_4N_2$ requires C, 65·0; H, 7·3; N, 8·4%). The fawn *methiodide*, prepared in methanol, had m. p. 175—180° (decomp.) (Found: C, 53·4; H, 6·5; I, 32·7. $C_{17}H_{27}N_2I$ requires C, 53·2; H, 6·5; I, 33·1%).

10-*Acetyl*-1 : 2 : 3 : 4-*tetrahydrobenzo*[b]*pyrrocoline* (XIX).—2-Dimethylamino*cyclo*hexanone [13] (36 g.) with 2-pyridylmethyl-lithium [14] by the usual method gave *2-dimethylamino*-1-*2'-pyridylmethyl*cyclo*hexanol* (XVIII) (31 g.), b. p. 140—150°/0·5 mm. (Found: C, 72·4; H, 8·9; N, 11·5. $C_{14}H_{22}ON_2$ requires C, 71·8; H, 9·4; N, 12·0%). This was boiled with acetic anhydride (300 ml.) for 6 hr. After removal of excess of anhydride the product was poured into water. A viscous oil separated which partially solidified. The aqueous layer (A) was decanted and the semi-solid was lixiviated with a little ether and filtered off. It crystallised from ethanol, to give the pyrrocoline (XIX) (3·5 g.), yellow needles, m. p. 154° (Arata [15] gives m. p. 152°) (Found: C, 79·0; H, 7·1; O, 7·6. Calc. for $C_{14}H_{15}ON$: C, 78·9; H, 7·1; O, 7·5%), $\lambda_{max.}$ 237, 274, 283, 364, and 380 (infl.) mμ (ε 26,000, 4400, 4000, 14,000, and 11,000). The aqueous layer (A) was basified and the liberated oil extracted with ether and distilled, the fraction having b. p. 125—132°/0·5 mm. being collected (Found: N, 6·3; Ac, 16·7. $C_{14}H_{17}O_2N$ requires N, 6·1; Ac, 18·5%), $\lambda_{max.}$ 242, 270, and 278 mμ (ε 8000, 5900, 5600).

4-Hydroxy-1-*methyl*-4-*2'-pyridylpiperidine* (XVI).—*N*-Methylpiperidone [16] (57 g.) reacted with 2-pyridyl-lithium in the usual way, giving a solid (47 g.), which, by crystallisation from light petroleum (b. p. 40—60°) and then from acetone, gave the *alcohol* (XVI) (35 g.) as large prisms, m. p. 84—85° (Found: C, 68·7; H, 7·9; N, 14·5. $C_{11}H_{16}ON_2$ requires C, 68·8; H, 8·3; N, 14·6%), $\lambda_{max.}$ 258 mμ (ε 3000). This (5 g.) and acetic anhydride (50 ml.) were boiled for 6 hr. After removal of the excess of anhydride the product was dissolved in water, basified, and extracted with ether three times, affording a solid (4·5 g.) which on crystallisation from light petroleum (b. p. 40—60°) gave *1-methyl-4-2'-pyridylpiperidin-4-yl acetate*, rods, m. p. 88—89°, depressed to 58—72° on admixture with the alcohol (Found: C, 67·2; H, 7·7; N, 11·9. $C_{13}H_{18}O_2N_2$ requires C, 66·7; H, 7·7; N, 12·0%). The product was very clean, and no pyrrocoline was detected by ultraviolet spectroscopy.

1 : 2 : 5 : 6-*Tetrahydro*-1-*methyl*-4-*2'-pyridylpyridine* (XVII).—Thionyl chloride (4·7 g.) in benzene (5 ml.) was added dropwise to the hydroxy-piperidine (XVI) (5 g.) in benzene (16 ml.) at 0°, and the mixture then boiled under reflux for 2 hr. Excess of thionyl chloride was removed *in vacuo*, and the residue treated with water, filtered, and evaporated *in vacuo*. The residue, recrystallised from ethanol, gave the tetrahydropyridine hydrochloride (4·5 g.), m. p. 200—202°. Analysis suggested that this was a mixture of mono- and di-hydrochlorides. The *base* had b. p. 148—151°/10 mm., m. p. 36—38° (Found: C, 75·6; H, 7·7; N, 16·5. $C_{11}H_{14}N_2$ requires C, 75·9; H, 8·0; N, 16·1%), $\lambda_{max.}$ 240 and 270 mμ (ε 7800 and 4300). After its submission to the usual cyclisation procedure, no pyrrocoline was detected in the product.

2-Phenyl-3-piperidino-1-*2'-pyridylpropan-2-ol*.—ω-Piperidinoacetophenone [17] (70 g.) with 2-pyridylmethyl-lithium [14] gave an oily undistillable propanol (103 g.). This was dissolved in ethanol (250 ml.) and treated with hydrogen chloride till just acid to Congo-red. Sufficient ether was added to produce a slight permanent turbidity, and the mixture left overnight. The solid (73 g.) was filtered off and recrystallised from ethanol, to give the *dihydrochloride* (63 g.), m. p. 188° (decomp.) (Found: C, 61·3; H, 7·5; N, 7·3; Cl, 18·7. $C_{19}H_{24}ON_2Cl_2$ requires C, 61·8; H, 7·1; N, 7·6; Cl, 19·3%). The *base*, crystallised from light petroleum (b. p. 40—60°), had m. p. 59—60° (Found: C, 77·1; H, 8·2; N, 9·4. $C_{19}H_{24}ON_2$ requires C, 77·1; H, 8·1; N, 9·5%), $\lambda_{max.}$ 259 (infl.), 263, and 267 (infl.) mμ (ε 4650, 5200, and 4250). After submission to cyclisation by the usual method, no pyrrocoline could be isolated from the product.

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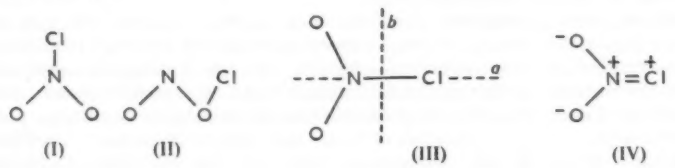
64. *The Microwave Spectrum, Structure, and Dipole Moment of Nitryl Chloride.*

By D. J. Millen and K. M. Sinnott.

Rotational transitions in the microwave spectra or $NO_2{}^{35}Cl$ and $NO_2{}^{37}Cl$ have been assigned and molecular rotational constants evaluated. Structural parameters $r_{NCl} = 1{\cdot}840$ Å, $r_{NO} = 1{\cdot}202$ Å and $\angle ONO = 130°\,35'$ are obtained. From the hyperfine structure of the spectra, chlorine nuclear quadrupole coupling parameters $eQ\,.\,\partial^2V/\partial a^2 = -94{\cdot}28$ Mc./sec., $eQ\,.\,\partial^2V/\partial b^2 = 51{\cdot}23$ Mc./sec., and $eQ\,.\,\partial^2V/\partial c^2 = 43{\cdot}05$ Mc./sec. were obtained for $NO_2{}^{35}Cl$; the corresponding values for $NO_2{}^{37}Cl$ are $-74{\cdot}45$, $40{\cdot}98$, and $33{\cdot}47$ Mc./sec. These coupling parameters have been interpreted to give information about the double-bond character of the nitrogen–chlorine bond. From a study of the Stark effect of the $0_{00}^{3/2} \longrightarrow 1_{01}^{5/2}$ transition the molecular dipole moment has been evaluated as $0{\cdot}42 \pm 0{\cdot}01$D.

Several compounds of the type NO_2X are well known. Crystalline salts [1] with ionic structures [2] $NO_2{}^+X^-$ are obtained for $X = NO_3^-$, $HS_2O_7^-$, FSO_3^-, $\frac{1}{2}S_2O_7^{2-}$, and $\frac{1}{2}S_3O_{10}^{2-}$. By contrast, for X = Cl or F the compounds are gaseous at room temperature. For nitryl chloride chemical evidence [3] has at different times been interpreted to support both structures (I) and (II).



(I) (II) (III) (IV)

The infrared spectrum [4] was interpreted on the basis of structure (I) although no decision between planar and non-planar possibilities was reached. The present study of the microwave spectrum has provided a clear argument [5] establishing the planar structure (I). We have now analysed the spectra of $NO_2{}^{35}Cl$ and $NO_2{}^{37}Cl$ to give values for internuclear distances and angles, and information about bond properties from nuclear quadrupole fine structure and the molecular dipole moment.

The Spectrum.—Many lines were observed in the region 8000—26,000 Mc./sec.; those which have been assigned to low-J transitions are listed in Tables 1 and 2. The spectrum has the features expected for the isotopic asymmetric rotors $NO_2{}^{35}Cl$ and $NO_2{}^{37}Cl$ with hyperfine structure due to quadrupole interaction of a single nucleus in each case. The magnitude of the splitting makes it clear that the chlorine nuclei are involved. No further splitting of these lines could be resolved; nuclear quadrupole interaction with ^{14}N was therefore ignored and the problem treated as one of rotational coupling with a single nucleus.

The multiplet 8876·26, 8899·90, and 8918·70 Mc./sec. was identified as a J, $0 \longrightarrow 1$ transition for $NO_2{}^{35}Cl$, the outer lines being displaced from the middle one in very nearly the ratio 4 : 5 expected for this transition when the splitting arises through rotational coupling with a single quadrupolar nucleus of spin $I = \frac{3}{2}$. Rotational transitions J, $1 \longrightarrow 2$ and J, $2 \longrightarrow 3$ having appropriate hyperfine structure were also identified. The

[1] Goddard, Hughes, and Ingold, *J.*, 1950, 2559.
[2] Millen, *J.*, 1950, 2610.
[3] Schmiesser and Gregor-Haschke, *Z. anorg. Chem.*, 1948, **255**, 33; Seel and Nogradi, *ibid.*, 1952, **269**, 188; Batey and Sisler, *J. Amer. Chem. Soc.*, 1952, **74**, 3408.
[4] Ryason and M. K. Wilson, *J. Chem. Phys.*, 1954, **22**, 2000.
[5] Millen and Sinnott, *Chem. and Ind.*, 1955, 538.

assignments are listed in Table 1, F_i and F_f being the initial and final values of the resultant angular momentum quantum number, $F = I + J$.

In the same way the multiplet 8644·60, 8663·20, and 8678·10 Mc./sec. was identified as the J, $0 \longrightarrow 1$ transition of the heavier isotopic species, $NO_2{}^{37}Cl$. The rotational lines assigned are given in Table 2.

TABLE 1. *Spectrum of* $NO_2{}^{35}Cl$. *Assignments, intensities, and comparison of observed and calculated frequencies.*

				Frequency (Mc./sec.)		
J	J'	F_i	F_f	Observed	Calculated	Intensity (cm.$^{-1}$)
0_{00}	1_{01}	3/2	3/2	8876·28	8876·27	5×10^{-8}
		3/2	5/2	8899·90	8899·87	$7{\cdot}5 \times 10^{-8}$
		3/2	1/2	8918·70	8918·75	$2{\cdot}4 \times 10^{-8}$
1_{01}	2_{02}	1/2	3/2	17,587·70	17,587·62	$1{\cdot}0 \times 10^{-7}$
		5/2	5/2	17,589·88	17,589·94	$1{\cdot}1 \times 10^{-7}$
		1/2	1/2	17,610·80	17,610·81	$1{\cdot}0 \times 10^{-7}$
		5/2	7/2	17,612·98	17,613·12	$4{\cdot}8 \times 10^{-7}$
		3/2	5/2	17,613·52	17,613·54	$2{\cdot}5 \times 10^{-7}$
		3/2	3/2	17,629·90	17,630·10	$1{\cdot}2 \times 10^{-7}$
		3/2	1/2	17,653·20	17,653·29	$1{\cdot}8 \times 10^{-8}$
2_{02}	3_{03}	7/2	7/2	25,964·70	25,964·86	$1{\cdot}5 \times 10^{-7}$
		1/2	3/2	25,981·40	25,981·35	$4{\cdot}2 \times 10^{-7}$
		3/2	5/2	25,982·15	25,981·99	$6{\cdot}6 \times 10^{-7}$
		7/2	9/2	25,987·44	25,987·39	$1{\cdot}5 \times 10^{-6}$
		5/2	7/2	25,988·15	25,988·04	$1{\cdot}0 \times 10^{-6}$
		5/2	5/2	25,998·40	25,998·65	$2{\cdot}1 \times 10^{-7}$
		3/2	3/2	26,004·63	26,004·56	$1{\cdot}5 \times 10^{-7}$
6_{24}	6_{25}	13/2	13/2	9973·90	9974·00	$4{\cdot}9 \times 10^{-8}$
		11/2	11/2		9974·51	$4{\cdot}4 \times 10^{-8}$
		15/2	15/2	9976·40	9976·16	$5{\cdot}5 \times 10^{-8}$
		9/2	9/2		9976·65	$4{\cdot}0 \times 10^{-8}$

TABLE 2. *Spectrum of* $NO_2{}^{37}Cl$. *Assignments, intensities, and comparison of observed and calculated frequencies.*

				Frequency (Mc./sec.)		
J	J'	F_i	F_f	Observed	Calculated	Intensity (cm.$^{-1}$)
0_{00}	1_{01}	3/2	3/2	8644·60	8644·59	$1{\cdot}7 \times 10^{-8}$
		3/2	5/2	8663·20	8663·22	$2{\cdot}5 \times 10^{-8}$
		3/2	1/2	8678·10	8678·12	$8{\cdot}0 \times 10^{-9}$
1_{01}	2_{02}	5/2	7/2	17,161·32	17,161·24	$1{\cdot}6 \times 10^{-7}$
		3/2	5/2		17,161·54	$8{\cdot}0 \times 10^{-8}$
2_{02}	3_{03}	7/2	7/2	25,337·90	25,338·00	$5{\cdot}0 \times 10^{-8}$
		1/2	3/2	25,351·20	25,351·09	$1{\cdot}4 \times 10^{-7}$
		3/2	5/2		25,351·57	$2{\cdot}2 \times 10^{-7}$
		7/2	9/2	25,356·00	25,355·85	$5{\cdot}0 \times 10^{-7}$
		5/2	7/2	25,356·50	25,356·33	$3{\cdot}5 \times 10^{-7}$
		5/2	5/2	25,364·30	25,364·66	$7{\cdot}0 \times 10^{-8}$
		3/2	3/2	25,369·80	25,369·42	$5{\cdot}0 \times 10^{-8}$
2_{21}	3_{21}	3/2	3/2	25,978·50	25,978·49	$3{\cdot}7 \times 10^{-8}$
		3/2	5/2		25,978·49	$1{\cdot}3 \times 10^{-7}$
		7/2	7/2	25,983·48	25,983·52	$3{\cdot}4 \times 10^{-8}$
		7/2	9/2		25,983·52	$3{\cdot}1 \times 10^{-7}$

Intensities in Tables 1 and 2 were evaluated for 300° K, pressure broadening of 5 Mc./sec. per mm. being assumed, since contributions to line breadth from unresolved nitrogen nuclear quadrupole effects made experimental determination difficult.

Molecular Structure.—The rotational constants A, B, and C for each molecule can in principle be determined from the frequencies of the three low-J transitions. This procedure is not entirely satisfactory here since none of these frequencies is very sensitive to changes in A, so it was important to include in the calculation another transition which would overcome this insensitivity. The transition $6_{24} \longrightarrow 6_{25}$ was identified for this purpose.

The frequency of this transition is readily related to the rotational constants of the molecule through the equation

$$E_{J_\tau} = \frac{A - C}{2} \cdot E_\tau(\kappa) + \frac{A + C}{2} \cdot J(J+1)$$

in which the asymmetry parameter $\kappa = (2B - A - C)/(A - C)$ and values of $E_\tau(\kappa)$ can be obtained from Turner, Hicks, and Reitwiesner's tables.[6]

The nuclear quadrupole coupling constants were evaluated from the first-order interaction energy which is given [7] in terms of the nuclear quadrupole moment Q and the field gradients along the inertial axes a, b, and c by

$$E_Q(J,F) = \frac{eQ}{J(J+1)}\left\{\left(\frac{\partial^2 V}{\partial a^2}\right)\left[J(J+1) + E(\kappa) - (\kappa+1)\left(\frac{\partial E(\kappa)}{\partial \kappa}\right)\right] + 2\left(\frac{\partial^2 V}{\partial b^2}\right)\left(\frac{\partial E(\kappa)}{\partial \kappa}\right) + \left(\frac{\partial^2 V}{\partial c^2}\right)\left[J(J+1) - E(\kappa) + (\kappa-1)\left(\frac{\partial E(\kappa)}{\partial \kappa}\right)\right]\right\} Y(F)$$

where

$$Y(F) = \frac{\frac{3}{4}C(C+1) - I(I+1)(J)(J+1)}{2(2J+3)(2J-1)(2I-1)(I)}$$

with

$$C = F(F+1) - I(I+1) - J(J+1)$$

Making use of the condition

$$\frac{\partial^2 V}{\partial a^2} + \frac{\partial^2 V}{\partial b^2} + \frac{\partial^2 V}{\partial c^2} = 0$$

and writing $\chi_{aa} = eQ\left(\frac{\partial^2 V}{\partial a^2}\right)$, etc., we can put the expression in a convenient form for computation:

$$E_Q(J,F) = \left\{(\chi_{aa} + \chi_{cc})\left[J(J+1) - 3\left(\frac{\partial E(\kappa)}{\partial \kappa}\right)\right] + (\chi_{aa} - \chi_{cc})\left[E(\kappa) - \kappa\left(\frac{\partial E(\kappa)}{\partial \kappa}\right)\right]\right\} \cdot \frac{Y(F)}{J(J+1)}$$

The rotational constants, and nuclear quadrupole coupling parameters calculated for the two isotopic species, are given in Table 3. The frequencies calculated from these six

TABLE 3. *Rotational constants and nuclear quadrupole coupling constants for* $NO_2{}^{35}Cl$ *and* $NO_2{}^{37}Cl$ *(all values are given in Mc./sec.).*

	A	*B*	*C*	χ_{aa}	χ_{bb}	χ_{cc}
$NO_2{}^{35}Cl$	13,239·9$_6$	5173·78	3721·37	−94·28	51·23	43·05
$NO_2{}^{37}Cl$	13,240·0	5019·00	3640·49	−74·45	40·98	33·47

TABLE 4. *Parameters relating to the momental ellipsoids of* $NO_2{}^{35}Cl$ *and* $NO_2{}^{37}Cl$. *I_a, I_b, I_c, and Δ are expressed in atomic mass units* $\times$ Å^2.

	I_a	I_b	I_c	Δ	κ
$NO_2{}^{35}Cl$	38·1822	97·710$_1$	135·845$_4$	−0·046$_9$	−0·694827
$NO_2{}^{37}Cl$	38·1821	100·723$_5$	138·863$_4$	−0·041$_6$	−0·712807

parameters for each species are listed in Tables 1 and 2 for comparison with the observed frequences. The agreement is satisfactory.

The rotational constants lead directly to molecular principal moments of inertia. These are listed in Table 4, which also includes the values calculated for the asymmetry parameter κ and the inertial defect $\Delta = I_a - I_b - I_c$.

[6] Turner, Hicks, and Reitwiesner, Ballistics Research Laboratories Report No. 878, reproduced in Townes and Schawlow, "Microwave Spectroscopy," McGraw-Hill, New York, 1955.

[7] Bragg and Golden, *Phys. Rev.*, 1949, **75**, 735.

For both isotopic species Δ is nearly zero, as required for a rigid planar body. The values of Δ are comparable with those observed for other planar molecules and can be safely attributed to zero-point motion. A further simple argument confirms planarity and establishes structure (I) conclusively. From the values of the rotational constants of $NO_2{}^{35}Cl$ it was calculated that the $1_{10} \rightarrow 2_{11}$ and $2_{12} \rightarrow 3_{13}$ transitions would be expected at 19,230 and 24,380 Mc./sec. respectively, both transitions being allowed by that component of dipole moment which permits the observed transitions. A careful search failed to reveal any lines which could be assigned to these transitions. Their absence is easily understood in terms of the planar structure (I), for which rotation about the two-fold axis along the nitrogen–chlorine bond interchanges identical oxygen atoms. In order that the total wave function be symmetric to this operation, the rotational wave functions must also be symmetric with respect to this operation for a molecule in even electronic and vibrational states. Thus the rotational states 1_{10}, 2_{11}, 2_{12}, and 3_{13} do not occur for planar structure (I) in its ground vibrational and electronic state, since they belong to the forbidden classes J_{0e} and J_{00}.

Internuclear distances and angles for the planar structure were evaluated from the rotational constants and are as follows: $r_{NCl} = 1{\cdot}840$ Å, $r_{NO} = 1{\cdot}202$ Å, and $\angle ONO = 130° 35'$. The inertial axes are shown in (III). Some idea of the uncertainties in the structural parameters due to zero-point vibrations can be obtained from the inertial defect. By assigning the whole of the inertial defect for $NO_2{}^{35}Cl$ to each principal moment of inertia in turn, it was found possible to fit any pair of principal moments by a structure falling in the range $r_{NCl} = 1{\cdot}840 \pm 0{\cdot}002$ Å, $r_{NO} = 1{\cdot}202 \pm 0{\cdot}001$ Å and $\angle ONO = 130° 35' \pm 15'$.

Further information about the nitrogen–chlorine bond has been obtained by interpreting the nuclear quadrupole fine structure. Nitryl chloride provides a particularly clear case for the estimation of double-bond character in this way. The analysis of the spectrum leads directly to the coupling coefficients along and perpendicular to the nitrogen–chlorine bond, and the usual assumptions about transformation of axes to evaluate coupling components along a bond direction from values along inertial axes are not required. Table 3 shows that the coupling constants along the *b* and *c* axes [see (III); *c* is orthogonal to *a* and *b*] are not identical. Thus there are different field gradients along the *b* and *c* axes at the chlorine nucleus. Evidently there is not axial symmetry about the nitrogen–chlorine bond as would be expected for an unperturbed σ bond.[8] The departure of the field gradient from axial symmetry is in the direction expected for electron loss from the $3p_c$ chlorine orbital. Such an electron loss is represented by a contribution to the ground state from the resonance structure (IV). The quantitative importance of this resonance structure has been calculated on the assumption that so far as chlorine nuclear quadrupole interactions are concerned the structure is equivalent to loss of an electron from the $3p_c$ chlorine atomic orbital.

The observed coupling coefficients χ_{aa}, χ_{bb}, and χ_{cc} along the directions of the inertial axes are given in Table 3. If the electron loss along the direction of the *c* axis contributes χ^e_{cc} to χ_{cc} then, according to Laplace's theorem, it makes a contribution of $-\frac{1}{2}\chi^e_{cc}$ to each of χ_{bb} and χ_{aa}. Thus $\chi^e_{cc} = \frac{2}{3}(\chi_{cc} - \chi_{bb})$ may be evaluated as $-5{\cdot}45$ Mc./sec. for $NO_2{}^{35}Cl$. Since the complete removal of an electron from a $3p_c$ atomic orbital for the chlorine atom leads to a coupling coefficient of $-109{\cdot}6$ Mc./sec., the value for χ^e_{cc} can be interpreted as indicating $5{\cdot}0\%$ electron deficit for the chlorine $3p_c$ orbital.

The interpretation of the coupling coefficient along the nitrogen–chlorine axis is not so clear because of the usual difficulty of separating contributions from ionic character $O_2N^+Cl^-$ and *s* character in the chlorine atomic orbital used in bond formation.[9] If the chlorine orbital is taken to be a pure *p* orbital, then, making the usual assumptions, we obtain a value of $11{\cdot}6\%$ ionic character.

[8] Goldstein and Bragg, *Phys. Rev.*, 1950, **78**, 347; Goldstein, *J. Chem. Phys.*, 1956, **24**, 106.
[9] Townes and Dailey, *ibid.*, 1949, **17**, 782; 1955, **23**, 118; Gordy, *Discuss. Faraday Soc.*, 1955, **19**, 14.

Dipole Moment.—The Stark effect of the transition J, $0_{00} \longrightarrow 1_{01}$; F, $3/2 \longrightarrow 5/2$, at 8899·90 Mc./sec. was studied quantitatively. The line is expected to give rise to two Stark components corresponding to $M_F = \pm\frac{1}{2}$ and $M_F = \pm\frac{3}{2}$ for the upper state. These were not resolved, their calculated separation at the highest voltage used being only 0·2 Mc./sec. The frequencies of the Stark component for various field strengths are given in Table 5.

TABLE 5. *Stark effect for the* $0_{00}^{3/2} \longrightarrow 1_{01}^{5/2}$ *transition.*

Field strength V (v/cm.)	0	723	822	907	988	1070
Frequency of Stark component (Mc./sec.)	8899·90	8900·90	8901·30	8901·75	8902·30	8902·80

The frequency displacements $\Delta\nu$ (Mc./sec.) of the single Stark component observed are fitted moderately well by $\Delta\nu = 0{\cdot}203\varepsilon^2$, values of ε in e.s.u. being obtained by calibration of the equipment by use of the Stark effect of the $J,1 \longrightarrow 2$ transition of carbonyl sulphide OCS which has a dipole moment [10] of $0{\cdot}7085 \pm 0{\cdot}004 \times 10^{-18}$ e.s.u.

Second-order perturbation theory [11] gives the following expressions for the two unresolved components:

$$M_F = \pm\tfrac{1}{2} \quad \Delta\nu = 1{\cdot}24 \times 10^{36}\mu^2\varepsilon^2$$
$$M_F = \pm\tfrac{3}{2} \quad \Delta\nu = 1{\cdot}09 \times 10^{36}\mu^2\varepsilon^2$$

where both μ and ε are in e.s.u. Both expressions satisfy the experimental result for $\mu = 0{\cdot}42 \pm 0{\cdot}01$ D.

EXPERIMENTAL

Spectra were observed by using a Stark-modulated spectrometer.[12] Absorption cells were made of 10 ft. lengths of copper X- and K-band waveguide, with a central strip electrode insulated by Teflon tape. Stark modulation voltages were applied by a 100 kc./sec. square-wave generator. Microwave power was detected by IN26 or CV253 crystals, and the 100 kc./sec. component amplified by a H.R.O. communications receiver. The output signal was either displayed on an oscilloscope or fed into a Brown recorder.

As microwave sources, 2K33 klystrons were used in the region 21,000—27,000 Mc./sec. and CV129 klystrons with modified cavities for the region 8000—11,000 Mc./sec. For observing spectra in the region 16,000—21,000 Mc./sec. a crystal doubler was constructed. A CV364 crystal was mounted in a holder across the X-band waveguide and provided with probes on either side of the crystal for matching. It was found important to adjust the depth of insertion of the crystal as well as the probe positions in order to obtain best operation. The method provided a simple and adequate source of power of the doubled frequency, and was found also to generate smaller amounts of the tripled frequency. The fundamental frequency was removed by use of appropriately-dimensioned filter sections. These and the necessary microwave transformer sections were prepared by electrodeposition of copper on machined formers, which were prepared from polystyrene coated with silver by evaporation. Finally the polystyrene was dissolved by sulphur-free benzene.

Approximate values of frequencies were obtained with wavemeters, several of which, utilising the TE_{011} mode and the coupling system suggested by Bleaney, Loubser, and Penrose,[13] were constructed. Three such meters were found to operate well over the ranges 7·5—9·5, 9·5—12·5, and 19—23 kMc./sec. The frequencies of lines were measured with a frequency standard constructed to have an accuracy of about 1 part in 10^7. The first stage consists of a 5 Mc./sec. electron-coupled oscillator, controlled by a quartz crystal operated at its inversion temperature in a thermostatically controlled oven. The frequency of this stage can be reduced by about 0·0001% by a trimming condenser in parallel with the crystal, and in this way the output can be adjusted to zero-beat with the standard 5 Mc./sec. signal from station MSF (operated by the National Physical Laboratory of Rugby). Successive stages of frequency multipliers raise the frequency through 20, 60, 180, to 540 Mc./sec. The multipliers are conventional

[10] Shulman and Townes, *Phys. Rev.*, 1950, **77**, 500.
[11] Golden and E. B. Wilson, jun., *J. Chem. Phys.*, 1948, **16**, 669; Fano, *J. Res. Nat. Bur. Stand.*, 1948, **40**, 215.
[12] McAfee, Hughes, and E. B. Wilson, jun., *Rev. Sci. Instr.*, 1949, **20**, 821.
[13] Bleaney, Loubser, and Penrose, *Proc. Phys. Soc.*, 1947, **59**, 185.

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except for the last stage which employs a QQVO3—20 valve operated with a quarter-wave parallel-line tuned input circuit, and in the plate circuit a butterfly resonant circuit of the type described by Karplus.[14] In order to obtain spectra of nitryl chloride it was necessary for the gas to flow through the cell continuously and to surround the wave-guide cell in solid carbon dioxide.

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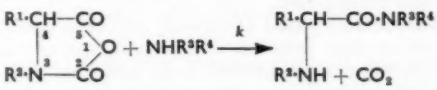
[14] Karplus, *Proc. Inst. Radio Eng.*, 1945, **33**, 426.

65. *Stereochemical Aspects of the Reactions between α-N-Carboxyamino-acid Anhydrides and Primary and Secondary Bases.*

By D. G. H. BALLARD and C. H. BAMFORD.

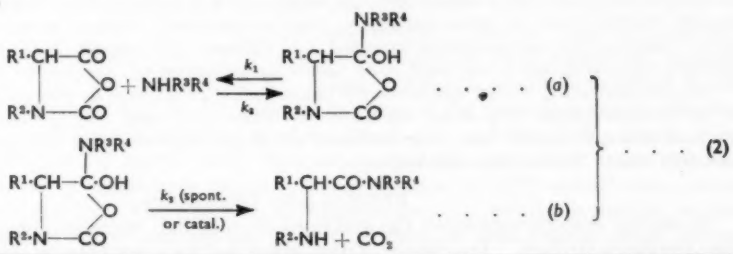
The bimolecular rate constants for the reaction between a number of substituted *N*-carboxyglycine anhydrides and three bases (glycine dimethylamide and derivatives of it) have been determined with a view to elucidating the steric course of the reactions. A substituent on the nitrogen atom in the anhydride ring causes steric interference which is particularly pronounced if the base carries an *iso*propyl group on the nitrogen atom. Substitution at position 4 reduces the rate of addition of a primary base at position 5 on the same side of the ring as the substituent; with a secondary base the effect is much greater. The configuration of the transition state is discussed; the observations are consistent with an approach to $C_{(5)}$ by the attacking base along a line passing over the ring-nitrogen atom slightly inclined to the plane of the ring. The fused rings in *N*-carboxy-L-proline anhydride confer a saucer-like shape on the molecule which results in a reduction of the steric interference mentioned above; this is reflected in higher rate constants.

POLYMERIZATION of the *N*-carboxy-anhydrides of α-amino-acids has been investigated in detail in recent years, and mechanisms have been advanced for the reactions initiated by amines and salts.[1] With primary and secondary bases the initiation and the propagation reactions are fundamentally similar, consisting of addition of a base molecule to the carboxyl group in position 5 followed by elimination of carbon dioxide:



(1)

In at least one instance this type of reaction is strongly catalyzed by anions of weak organic acids, including carbamic acids, but when this complication is absent the reactions are of first order in anhydride and base.[2] The general mechanism may be written in the annexed form.



(2)

[1] For a summary and references see Bamford, Hanby, and Elliott, "Synthetic Polypeptides," Academic Press, New York, 1956, Chap. III.
[2] Ballard and Bamford, unpublished work.

Two extreme cases are encountered; in one (exemplified by *N*-carboxysarcosine anhydride) the equilibrium in (2*a*) is effectively established and (2*b*) is rate-determining, while in the other (of which *N*-carboxy-DL-phenylalanine anhydride is an example) the reaction in (2*a*) appears to be rate-controlling.[3]

Different anhydrides polymerize at very different rates, and in particular those with substituents on the nitrogen and at position 4 frequently fail to polymerize when treated with any type of initiator. The *N*-carboxy-anhydride derived from α-methylalanine (" α-amino*iso*butyric " acid) is a good example; this does not polymerize at room temperatures when treated with amines, salts of weak organic acids, or sodium methoxide. As in this case, the substituents are usually saturated and comparatively non-polar and are therefore unlikely to produce pronounced changes in electron density, so it appears that their influence on reactivity is predominantly steric. We describe in this paper an investigation in which the substituents in the *N*-carboxy-anhydride and the attacking base were varied in a systematic manner, with the object of elucidating the steric features of the reactions. For this purpose concentrations of base at least equal to those of the anhydride were used; little polymerization then occurs if the initiating base and the base resulting from reaction (1) have comparable strengths, and the observed rates correspond closely to those of the initiation reaction. In all cases except proline the DL-anhydride was used. The observed differences in rate are discussed in terms of the dependence of the velocity coefficient k_1 on steric factors.

Experimental

Materials.—The *N*-carboxy-anhydrides were prepared from the α-amino-acids by standard methods which have been summarized elsewhere.[3] They were purified by recrystallization until the chloride content was less than 0·05%, then sublimed and used immediately. The sublimed materials contained no detectable chloride.

The bases used were glycine dimethylamide and substituted derivatives ($R^4 = CH_2{\cdot}CO{\cdot}NMe_2$, in all cases). They were made by two methods. In the first the appropriately substituted *N*-carboxy-glycine anhydride was treated with a large excess of liquid dimethylamine. Excess of the latter was distilled off and the residual oil fractionated in vacuum. In the second method chloroacetyl chloride with dimethylamine yielded α-chloro-*NN*-dimethylacetamide,[4] which was treated with a 33% w/v solution of the appropriate amine for 3 days at room temperature. The base was isolated by fractionation. The equivalent weights of the amines were determined and the b. p.s agreed with those recorded.[5] Elementary analysis gave results in satisfactory agreement with those calculated.

The purification of nitrobenzene, used as solvent, has been described elsewhere.[3]

Technique.—The reactions were followed by the evolution of carbon dioxide, essentially as described earlier.[3] The normal precautions were taken to exclude water; none of the reactants was allowed to come into contact with atmospheric moisture, and the reaction vessel containing the anhydride and the base solution in separate compartments was prepared in a dry-box.

The " initial " rates, corresponding to conversions of 5% or less, were measured. The rates were usually almost constant over this range, and it is unlikely that the pressure of carbon dioxide formed would be great enough to have a significant catalytic effect on the reaction rates. Many of the reactions were too rapid to be followed conveniently in the simple constant-pressure apparatus which was used in an earlier investigation of catalysis by carbon dioxide.[3]

The concentration of base was measured before and after reaction by potentiometric titration of the solution diluted with about ten times its volume of alcohol. In all cases the initial and the final concentration of base were the same within experimental error, except when reaction was very slow. This is discussed below.

Results and Discussion

In all the systems examined the reactions were of first order in anhydride and base over the range studied. The Figure, a first-order plot for a typical run, shows that, while

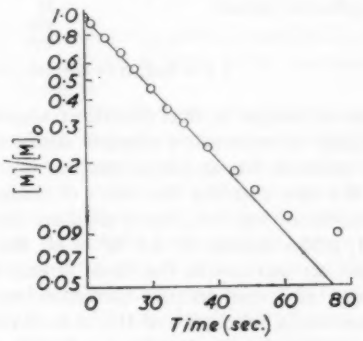
[3] Ballard and Bamford, *Proc. Roy. Soc.*, 1954, *A*, **223**, 495.
[4] Freudenberg and Markert, *Ber.*, 1927, **60**, 2447.
[5] Waley and Watson, *Proc. Roy. Soc.*, 1949, *A*, **199**, 499.

the rate constant for the initial reaction can be determined unambiguously, the reaction eventually departs from first-order dependence on anhydride concentration on account of the increasing importance of the propagation reaction.[3] Usually the anhydride and base concentrations were varied over an eight-fold and a five-fold range respectively; these represent the extremes which can be used with the present apparatus. Typical results are shown in Table 1 in which $[M]_o$, $[X]_o$ are the initial anhydride and base concentration and k the overall second-order constant. This constant will, in the limiting cases, be either k_1k_3/k_2 or k_1 [see equation (2)]. For present purposes distinction between the various cases is unnecessary since we are attributing the major differences observed to changes in k_1.

TABLE 1. *Reaction of* N-*carboxy*-N-*methyl*-DL-*alanine anhydride* ($R^1 = R^2 = Me$) *with glycine dimethylamide* ($R^4 = CH_2{\cdot}CO{\cdot}NMe_2$, $R^3 = H$) *in nitrobenzene at* 15°.

$10^2[M]_o$ (mole l.$^{-1}$)	9·00	5·46	4·92	2·66	2·29	1·08
$10^2[X]_o$ (mole l.$^{-1}$)	10·6	4·93	10·6	1·92	4·93	1·92
k (mole^{-1} l. sec.$^{-1}$)	0·43	0·45	0·44	0·45	0·45	0·48
		Mean 0·45				

The rate constants for the various anhydrides and bases are collected in Table 2; the extreme deviations from the mean values are shown; *N*-carboxyglycine anhydride is not



Reaction of N-*carboxy*-N-*methyl*-DL-*alanine anhydride with glycine dimethylamide in nitrobenzene at* 15°.
$[M]_o = 9{\cdot}0 \times 10^{-2}$ mole l.$^{-1}$; $[X]_o = 10^{-2}$ mole l.$^{-1}$.

included since its behaviour is in some ways abnormal and is insufficiently understood for kinetic analysis.

In discussing these results it is first necessary to consider the configuration of the *N*-carboxy-anhydride ring. In the absence of complicating factors the five-membered ring would be expected to be planar, with the N–R^2 bond and the carbonyl-oxygen atoms in the plane of the ring. The group R^1 would, of course, lie on one or other side of this plane, its position being determined by the asymmetry at the carbon atom $C_{(4)}$. This configuration would be expected to be the stable one if $R^1 = R^2 = H$. When $R^1 = R^2 =$ Me the situation is different. If the ring were planar some repulsion would be expected between R^2 and the neighbouring CO group, which would be in a completely eclipsed conformation, and also between R^1 and R^2. These repulsions would be relieved if the N–R^2 bond were to depart slightly from the mean plane of the ring; this might arise, for example, by a small amount of rotation about the $C_{(2)}$–N and the N–$C_{(4)}$ bond. The centres of the two methyl groups would then lie on opposite sides of the mean plane of the ring. A greater deviation from planarity would be expected if R^1 and R^2 were groups more bulky than methyl. The molecule of *N*-carboxyproline anhydride consists of two fused five-membered rings, and models show that there is considerable strain in the structure. Both the $C_{(4)}$–R^1 and the N–R^2 bond deviate from the mean plane of the anhydride ring in the same sense, and the whole molecule has a saucer-like shape. If a pyramidal nitrogen atom is used it is possible to construct two configurations; one of

TABLE 2. *Reactions between* N*-carboxy-anhydrides and bases in nitrobenzene at* 15° ($R^3 = CH_2{\cdot}CO{\cdot}NMe_2$).

N-Carboxy-anhydride R^1	R^2	Base R^3	k (mole^{-1} l. sec.$^{-1}$)	Rates * of addition on two sides of ring: same side as R^1	side opposite to R^1
Me	H	H	1·13 ± 0·10	m	n
		Me	0·48 ± 0·02	s	n
		Pr^i	0·10 ± 0·01	vs	m
H	Me	H	0·82 ± 0·03	n	
		Me	0·57 ± 0·03	n	
		Pr^i	$7{\cdot}4 \times 10^{-4}$	s	
Me	Me	H	0·45 ± 0·02	m	m
		Me	0·16 ± 0·03	s	m
		Pr^i	2×10^{-5}	vs	vs
Ph·CH$_2$	H	H	1·0 ± 0·2	m	n
		Me	0·40 ± 0·07	s	n
		Pr^i	0·30 ± 0·02	vs	m
H	Pr^i	H	0·83 ± 0·03	n	
		Me	0·48 ± 0·04	n	
		Pr^i	$< 10^7$	vs	
α-*N*-Carboxyamino-α-methylalanine anhydride		H	0·29 ± 0·05	m	
		Me	$8{\cdot}4 \times 10^{-4}$	s	
		Pr^i	1×10^{-6} approx.	vs	
N-Carboxy-L-proline		H	2·68 ± 0·08	vs	f
		Me	2·00 ± 0·07	vs	f
		Pr^i	0·12 ± 0·02	vs	m

* f = fast, n = normal, m = medium, s = slow, vs = very slow.

these is similar to that described above, while the other is so highly strained that it is unlikely to represent a possible configuration of the molecule. The saucer-like shape of the molecule has an important bearing on its reactivity, as will appear below.

We now consider the effect of changes in R^3 on the bimolecular rate constant. The strengths of the three bases used are not very different, the pK_b values at 20° being 5·67, 5·21, 5·32 respectively for $R^3 = H$, Me, and Pr^i. It is known that, other things being equal, an increase in the basic strength leads to an increase in the rate of reaction,[1] a change of 1 unit in pK_b corresponding to a factor of 3 approximately. The extreme difference in reactivity of the three bases attributable to changes in basic strength alone should therefore be less than a factor of 2. From Table 2 we see that if $R^1 = Me$ and $R^2 = H$, the change of R^3 from H to Pr^i leads to a reduction in the rate constant by a factor of 10 approximately. This is in a direction opposite to that expected from considerations of basic strength, and indicates that steric interference plays a part when $R^3 = Pr^i$. Similar considerations apply to the reactions of *N*-carboxy-DL-phenylalanine anhydride ($R^1 = Ph{\cdot}CH_2$, $R^2 = H$) with the three bases. The important point is that the presence of an *iso*propyl group in the base does not, by itself, cause a very large reduction in rate (*i.e.*, a reduction $\gg$ ten-fold). If now we consider the anhydride with $R^1 = R^2 = Me$, we see that if $R^3 = H$ or Me the rates are somewhat lower than those already considered for $R^1 = Me$, $R^2 = H$—by a factor less than 4—but if $R^3 = Pr^i$ the rates in the two cases differ by a factor of 5000. From the foregoing it will be clear that this cannot be an electronic effect, but can only be the result of steric interference involving the methyl group on the nitrogen atom in the ring and the *iso*propyl group in the base. A similar conclusion may be reached by comparing the rate constants for $R^1 = H$ and $R^2 = Me$ or Pr^i. Change of R^2 from Pr^i to Me produces no change in rate if $R^3 = H$, and it reduces the rate constant only slightly if $R^3 = Me$; however it decreases the rate by a factor of more than 1000 if $R^3 = Pr^i$. Here again there must be interference between bulky substituents on the nitrogen atom in the ring and in the base.

This interference must occur in the transition state and therefore implies that the base approaches $C_{(5)}$ along a path which is slightly inclined to the plane of the ring and passes more or less directly above (or below) the nitrogen atom in the ring. This is the path

which is most nearly collinear with the bond that is being broken, *i.e.*, one of the carbonyl $C_{(5)}$–O bonds. It will be recalled that in simple bimolecular nucleophilic displacements the reagent approaches along a line which coincides in direction with the bond being broken; in the transition state the other three bonds of the carbon atom at which the displacement occurs are in a plane perpendicular to this direction, the attacking and the displaced group being on opposite sides of this plane. In the present case the direction of approach is therefore similar to that found in simple nucleophilic substitution, although the configuration of the transition state must necessarily be different since the bond being broken is part of a double bond, and the other bonds of the carbon atom concerned are part of a ring system. We therefore believe that in the transition state the nitrogen atom of the attacking base is located between $C_{(5)}$ and the nitrogen atom in the anhydride ring, with its centre above the plane of the ring. An examination of models reveals that with this arrangement considerable interference between R^2 and R^3 is possible if these are bulky groups. A further point to note is that the oxygen atoms of the carbonyl groups of the anhydride carry a negative charge, and therefore tend to resist the approach of the nitrogen of the attacking base, since this will be the negative pole of the C–N dipole. The nitrogen atom in the ring will, on the other hand, carry a positive charge, and the region of lowest electron density presumably lies between this atom and $C_{(5)}$. The suggested line of attack may therefore represent the most favourable direction of approach to $C_{(5)}$ on purely electrostatic considerations.

The suggested transition state will always involve a restriction on the rotation of alkyl groups attached to the basic nitrogen atom, and this will be at least partly responsible for the low frequency factors observed for these reactions.[1]

We now discuss the effects of substitution at $C_{(4)}$. A 4-methyl group necessarily gives rise to steric interference in the transition state which is particularly severe when the attacking base is secondary. In fact, addition of these bases to $C_{(5)}$ on the same side of the ring as the methyl group appears to be very difficult. The reaction of primary bases is affected to a much smaller extent. These points are illustrated by the behaviour of α-*N*-carboxy-α-methylalanine anhydride, in which $C_{(4)}$ carries two methyl groups and $R^2 = H$. This anhydride reacts with a primary base at a rate which is approximately one quarter of that obtained when $C_{(4)}$ carries only one methyl group and $R^2 = H$ (Table 2). A 4-methyl group therefore appears to reduce the rate of addition of a primary base to $C_{(5)}$ *on the same side of the ring* by a factor of about 7. The rate of addition of secondary bases is clearly reduced to a very much greater extent.

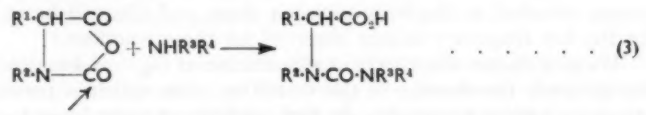
If addition on the side of the ring remote from R^1 were unaffected the maximum reduction in the overall rate constant which could be produced by a bulky substituent on $C_{(4)}$ would amount to a factor of 2. We have already seen, however, that if R^1 and R^2 are alkyl groups their centres will lie on opposite sides of the mean plane of the ring, and as a consequence addition to $C_{(5)}$ may be obstructed on both sides of the ring. It would be expected, therefore, that the introduction of a bulky group on $C_{(4)}$ might lead to a reduction in rate constant greater than that mentioned above if R^2 is other than H, particularly if the attacking base is secondary. These ideas are borne out of the results in Table 2. When $R^2 = Me$, $R^3 = H$, replacing $R^1 = H$ by $R^1 = Me$ reduces the rate constant by a factor of nearly 2. In this case the base is primary and the overall addition is not greatly impeded by R^1 or R^2. However, when $R^3 = Me$ or Pr^i the corresponding changes are greater, amounting to factors of 3·5 and 37 respectively. Here addition on the same side as R^1 is very greatly reduced, while addition on the other side is impeded by the projecting R^2 group.

It is interesting that, with $R^2 = Me$, the velocity constant falls off much more rapidly in passing from $R^3 = Me$ to $R^3 = Pr^i$ when $R^1 = Me$ than when $R^1 = H$. This is a further indication of the effect of a 4-methyl substituent, causing a departure of the N–R^2 bond from the plane of the ring. The resulting obstruction to addition on the side of the ring away from R^1 naturally increases with the size of R^3.

N-Carboxy-L-proline anhydride introduces some new features. The strain in the molecule may account in part for the relatively fast reaction of this anhydride with glycine and sarcosine dimethylamides (R^3 = H or Me respectively), the reactions being 6—12 times faster than those with *N*-carboxy-*N*-methyl-DL-alanine anhydride ($R^1 = R^2$ = Me). The last anhydride is structurally similar to the proline derivative except that no second ring is present. This conclusion will only hold if the kinetics are of the " sarcosine " type, *i.e.*, if the rate is proportional to the rate of decomposition of the complex formed between the anhydride and the base. In this case the strain in the ring might increase k_3 [equation (2)] and hence the overall rate constant. The molecule being saucer-shaped, attack at $C_{(5)}$ from the convex side of the saucer should occur comparatively readily since obstruction by the substituents on the nitrogen and $C_{(4)}$ is relatively small. Approach of the base along a path almost collinear with a $C_{(5)}$–O bond is in fact possible. This is probably the explanation of the relatively fast reaction of this anhydride with *N-iso*propylglycine dimethylamide (R^3 = Pr^i), whose rate constant is approximately 6000 times that of the corresponding reaction with the *N*-methyl-DL-alanine derivative.

The rates of addition of the bases on the two sides of the rings of the various anhydrides are summarized qualitatively in the right-hand portion of Table 2.

The decrease (see above), during the slow reactions, in the base content of the system may amount to as much as 20%. In these cases addition at $C_{(5)}$ is greatly hindered and addition at $C_{(2)}$ may take place, with formation of a ureido-derivative and a consequent reduction in the free base concentration:



. . . . . (3)

This reaction may not be a carbonyl addition, and its steric course may therefore be different from that for attack at $C_{(5)}$. For example, the base may approach in the direction $C_{(2)}$–$O_{(1)}$ shown by the arrow. When there is no steric restriction on the addition at $C_{(5)}$ reaction (3) occurs only to a very small extent at room temperature since it has a higher activation energy than reaction (1). It is, however, detectable at high temperatures, and constitutes a termination reaction in the polymerization of *N*-carboxy-anhydrides under these conditions.[6]

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[*Received, July 18th,* 1957.]

[6] Sela and Berger, *J. Amer. Chem. Soc.*, 1953, **75**, 6350; 1955, **77**, 1893.

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66. *Studies in Relation to Biosynthesis. Part XIII.* Griseofulvin.*

By A. J. BIRCH, R. A. MASSY-WESTROPP, R. W. RICKARDS, and HERCHEL SMITH.

Me·$^{14}CO_2H$, when fed to a strain of *Penicillium griseofulvum* Dierckx, leads to griseofulvin with the isotopic distribution shown in (I). This result supports the general validity of the acetic acid hypothesis. A preliminary account of some of this work has already appeared.[1]

STRUCTURAL evidence reviewed in Part I [2] suggested that the skeletons of many natural phenolic compounds are derived, at least in part, by the head-to-tail linkage of acetic

* Part XII, Birch, Pride, and Smith, *J.*, 1957, 5096.

[1] Birch, Massy-Westropp, Rickards, and Smith, *Proc. Chem. Soc.*, 1957, 98.

[2] Birch and Donovan, *Austral. J. Chem.*, 1953, **6**, 360.

acid units. The complete skeletons of anthraquinones related to emodin and of depsides related to orsellinic acid, and the phloroglucinol ring of plant pigments such as cyanidin and quercetin, probably arise in this way. Two types of ring-closure can be distinguished: an aldol type leading to a variety of structures, notably to orcinol derivatives, and a *C*-acylation type leading notably to phloroglucinol derivatives. This hypothesis was later used to assist structural investigations and has already predicted the correct one of several possible formulæ for eleutherinol,[3] flaviolin,[4] mellein,[5] α- and β-sorigenin,[6] and nalgiovensin.[7] Biochemical evidence in support of the hypothesis was obtained [8] by feeding $Me\cdot{}^{14}CO_2H$ to a strain of *Penicillium griseofulvum* Dierckx; the resulting 2-hydroxy-6-methylbenzoic acid was shown to have the isotopic distribution (II) (an asterisk denotes ^{14}C).

We have now examined the incorporation of $Me\cdot{}^{14}CO_2H$ into griseofulvin (I), produced by another strain of *P. griseofulvum* (L.S.H. Cat. No. P. 38). This substance contains a phloroglucinol ring and a (potential) orcinol ring and its formation from acetic acid would involve both types of ring-closure. The griseofulvin was degraded as outlined below, and the intensities of radioactivity of the products measured by Popjak's method.[9] We found it advantageous to express the activities of the compounds obtained in a series of degradations as the products of the molecular weights and the counts per 100 seconds of 1 cm.^{2} of substance at " infinite " thickness; these quantities are linearly proportional to the molar activities and we term them the relative molar activities. They are proportional to the number of labelled carbon atoms per molecule, which can therefore be calculated from the relative molar activity of griseofulvin on the assumption that it contains seven ^{14}C. These values are shown in the chart. It may be noted that the sum of the relative molar activities of any complete set of degradation products should be identical with that of the original substance. In these experiments the maximum statistical counting error is considered to be ±3%. From the results (see Experimental section) it appears that no other systematic errors are involved. The results prove the isotopic distribution (I) and lead to confidence in the general validity of the acetic acid hypothesis.

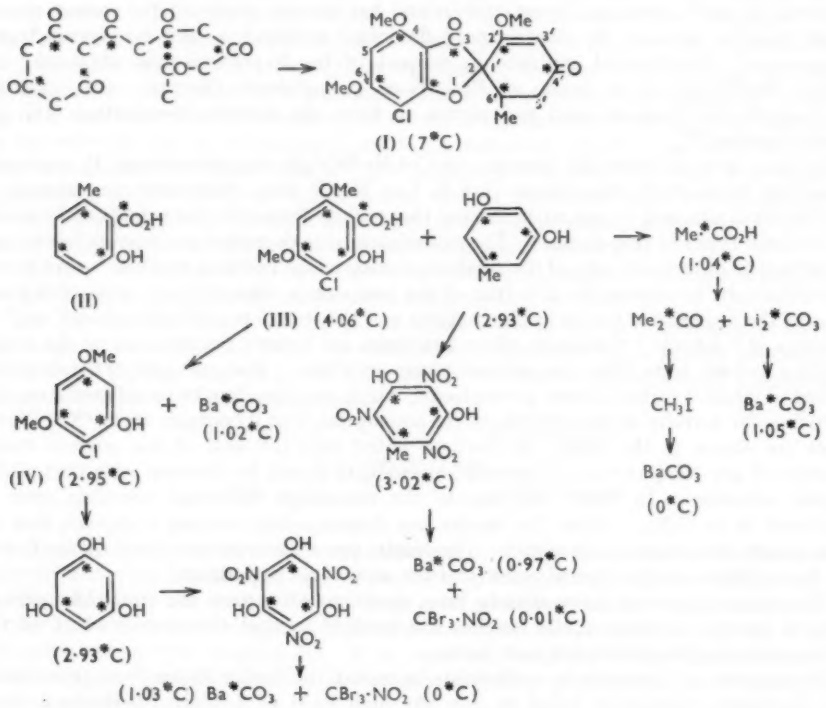
The methoxyl groups have already been shown to arise from the usual biochemical C_1-donor system (experimentally choline was used),[10] so that the sources of all of the carbon atoms in griseofulvin are now known.

Degradations of Griseofulvin.—Attempts to repeat the earlier fission [11] of griseofulvin with 2N-sodium methoxide failed to give the high yield of 3-chloro-2-hydroxy-4 : 6-dimethoxybenzoic acid (III) claimed, and the reaction was found to be sensitive to traces of water. Under our best conditions 35% of the acid (III) was obtained, together with an uncrystallisable gum. Fusion of griseofulvin with potassium hydroxide is known [12, 13] to give orcinol (74%), and this reaction was applied to the gum from the above reaction, producing a further quantity of the acid (52% total) and orcinol (85%). Direct fusion of griseofulvin gave a lower yield of the acid, and the two-stage process is advantageous.

The acid (III) was best decarboxylated by heat in the presence of glass wool, 2-chloro-3 : 5-dimethoxyphenol (IV) being obtained in 81% yield. Attempts were made to obtain phloroglucinol directly by heating the acid with acetic–hydriodic acid, but although decarboxylation was very rapid only a polymer resulted. The acid (III) was readily

[3] Birch and Donovan, *Austral. J. Chem.*, 1953, **6**, 372.
[4] *Idem, Chem. and Ind.*, 1954, 1047; *Austral. J. Chem.*, 1955, **8**, 529; Davies, King, and Roberts, *J.*, 1955, 2782; *Chem. and Ind.*, 1954, 1110.
[5] Blair and Newbold, *Chem. and Ind.*, 1955, **93**; *J.*, 1955, 2871.
[6] Haber, Nikuni, Schmid, and Yai, *Helv. Chim. Acta*, 1956, **39**, 1654.
[7] Birch and Massy-Westropp, *J.*, 1957, 2215.
[8] Birch, Massy-Westropp, and Moye, *Austral. J. Chem.*, 1955, **8**, 539.
[9] Popjak, *Biochem. J.*, 1950, **46**, 560.
[10] Hockenhull and Faulds, *Chem. and Ind.*, 1955, 1390.
[11] Grove, MacMillan, Mulholland, and Rogers, *J.*, 1952, 3977.
[12] Oxford, Raistrick, and Simonart, *Biochem. J.*, 1939, **33**, 240.
[13] Grove, MacMillan, Mulholland, and Rogers, *J.*, 1952, 3949.

dechlorinated by the action of Raney alloy and alkali,[14] giving 2-hydroxy-4 : 6-dimethoxybenzoic acid almost quantitatively. However, again extensive polymerisation occurred on attempted demethylation with 10N-hydrochloric acid.



Dechlorination of the phenol (IV) by the same method gave phloroglucinol dimethyl ether which was also unexpectedly sensitive to concentrated hydrobromic acid. Demethylation in 86% yield to phloroglucinol was accomplished with 5N-hydrochloric acid. The phloroglucinol was nitrosated [15] and the potassium salt of trinitrosophloroglucinol directly oxidised with hydrogen peroxide to trinitrophloroglucinol.[16] Fission of this substance with barium hypobromite gave the hydroxyl-carrying carbon atoms from positions 4, 6, and 7*a* as barium carbonate (2·16 mols.), and those from positions 3*a*, 5, and 7 as bromopicrin (2·46 mols.), further oxidised to barium carbonate. Trinitro-orcinol was degraded similarly, except that only two carbon atoms (positions 4′ and 2′) appear as carbon dioxide (1·84 mols.). It was more convenient not to isolate the acetic acid formed in this experiment but to produce it directly from orcinol itself by a Kuhn–Roth oxidation. The acetic acid was then converted into acetone and lithium carbonate by pyrolysis.[17] Contrary to records,[18] no interchange of carboxyl- and methyl-carbon atoms was observed in this pyrolysis, the barium carbonate from the methyl group being completely inactive.

[14] Schwenk, Papa, Whitman, and Ginsberg, *J. Org. Chem.*, 1944, **9**, 1.
[15] Freudenberg, Fikentscher, and Wenner, *Annalen*, 1925, **442**, 309.
[16] Cf. Travagli, *Atti Accad. sci. Ferrara*, 1949—50, **27**, 3; *Chem. Abs.*, 1951, **45**, 7544
[17] Cornforth, Hunter, and Popjak, *Biochem. J.*, 1953, **54**, 597.
[18] Popjak, Hunter, and French, *ibid.*, 1953, **54**, 238.

Experimental

Radioactive Assay.—Specimens were assayed for radioactivity with an end-window counter as infinitely thick, solid samples of 1 cm.^{2} cross-sectional area,[9] and counting rates were corrected for background and dead time of the instrument. Counting-equipment consisted of an EKCO Automatic Scaler Type N530D, in conjunction with an EKCO Probe Unit Type N558 and an EHM2S Geiger tube. The counts per 100 sec. were determined by recording the time required for 10^4 counts to be aggregated. Hence the statistical counting error is no greater than $3/\sqrt{10^4}$, *i.e.*, 3%. Estimates of absolute activity (where required) were obtained by comparison with a disc of radioactive poly(methyl methacrylate) (Amersham) of nominal specific activity 1 μc/g., counted under identical geometrical conditions. Other errors could be introduced by variations in packing or through the different constitutions of the substances being examined. In practice, no such errors could be distinguished.

Isolation of [^{14}C]*Griseofulvin.*—*Penicillium griseofulvum* Dierckx (London School of Hygiene Catalogue No. P. 38) was grown under the conditions described previously.[12] Preliminary experiments had shown that little mycelianamide and griseofulvin were produced until after about 14 days, production then increasing considerably. Accordingly, after 18 days' growth, a solution of sodium [*carboxy*-^{14}C]acetate (1·0 mc; 7·6 mg.) was distributed evenly among 8 flasks, each containing 350 ml. of medium. After a further 9 days' growth the products were isolated as recorded [12] and the residues chromatographed on acid alumina [13] to obtain a further small quantity of griseofulvin. Griseofulvin (0·2 g.) and mycelianamide (1·2 g.), m. p. 168—170°, resulted on crystallisation. This impure griseofulvin (100 mg.) was diluted 50 times with purified inactive material and recrystallised from ethanol, yielding colourless crystals, m. p. 219—220° (4·64 g.) [Found: relative molar activity × 10^{-3}, 417].

The yield in terms of incorporation of [*carboxy*-^{14}C]acetate was about 1%, 9·6 μc of [^{14}C]-griseofulvin being isolated. The yield has been previously erroneously given by us as 10%.[1]

Alkali Fission of Griseofulvin.—Griseofulvin (500 mg.) in 2N-sodium methoxide (50 ml.) was refluxed for 2·25 hr. under nitrogen. The cooled solution was poured into water (60 ml.) and acidified with hydrochloric acid, and the 3-chloro-2-hydroxy-4 : 6-dimethoxybenzoic acid (106 mg.) was filtered off. The gum (370 mg.) obtained by ether-extraction of the filtrate was mixed with potassium hydroxide (1·4 g.) and water (0·6 ml.) in a nickel crucible and heated under nitrogen at 160°. The temperature was raised to 220° during 15 min. and kept at 220—230° for 70 min. The residue, on cooling, was dissolved in water, and the solution saturated with carbon dioxide and ether-extracted. The precipitate (79 mg.) obtained on acidification of the aqueous layer was combined with the 3-chloro-2-hydroxy-4 : 6-dimethoxybenzoic acid obtained earlier and recrystallised from ethyl acetate, as colourless crystals (52%), m. p. 220—222° (decomp.), which were assayed for ^{14}C [Found: relative molar activity × 10^{-3}, 242; 4*C requires 238].

The ether extract of the bicarbonate solution was dried (Na_2SO_4) and evaporated to a gum, which sublimed at 110—120°/0·05 mm. The sublimate was crystallised from benzene–light petroleum (b. p. 40—60°), then from benzene, and resublimation gave orcinol, m. p. 106—107° (148 mg., 85%) [Found: relative molar activity × 10^{-3}, 175; 3*C requires 179].

2 : 4 : 6-*Trinitro-orcinol.*—To orcinol (164 mg.) dissolved in concentrated sulphuric acid (0·6 ml.) was added with stirring during 5 min. at 0° an ice-cold mixture of concentrated nitric acid (0·4 ml.) and concentrated sulphuric acid (0·8 ml.). Further concentrated nitric acid (0·65 ml.) was added, and after 40 min. at room temperature the mixture was poured into ice and water. 2 : 4 : 6-Trinitro-orcinol was filtered off and recrystallised from water as yellow needles, m. p. 171—172° (decomp.) (274 mg., 80%) (lit., m. p. 162° [19] and 163·5° [20]) [Found: relative molar activity × 10^{-3}, 180; 3*C requires 179]. An inactive specimen was analysed (Found: C, 32·3; H, 2·3; N, 16·0. Calc. for $C_7H_5O_8N_3$: C, 32·4; H, 2·0; N, 16·2%).

Hypobromite Degradation of 2 : 4 : 6-*Trinitro-orcinol.*—(a) *The nitro-carrying carbon atoms.* To trinitro-orcinol (131 mg.) in hot water (10 ml.) was added a hot solution of hydrated barium hydroxide (0·32 g.) in water (8 ml.). The stirred barium salt suspension was cooled to 0°, and an ice-cold solution of barium hypobromite [from bromine (0·4 ml.) and barium hydroxide (2·0 g.) in water (50 ml.)] was added. After 1 hour's stirring at room temperature, the bromopicrin was separated by steam-distillation and collected with ether. Evaporation, after washing

[19] Stenhouse, *J.*, 1871, 357.
[20] Merz and Zetter, *Ber.*, 1879, **12**, 2038.

of the extract with water and drying (Na_2SO_4), left the bromopicrin as a colourless liquid (395 mg., 88%). Van Slyke–Folch oxidation [21] of the bromopicrin gave barium carbonate, which was collected and washed by centrifugation for radioactive assay [Found: relative molar activity $\times 10^{-3}$, 0·6].

(b) *The hydroxyl-carrying carbon atoms.* Carbonate-free solutions were used throughout with a stream of nitrogen free from carbon dioxide and a soda-lime tube to exclude atmospheric contamination. The barium salt formed from trinitro-orcinol (43 mg.) and barium hydroxide (0·32 g.) was stirred with barium hypobromite solution [from bromine (0·16 ml.) and barium hydroxide (1·6 g.) in water (40 ml.)]. After 1 hr. a centrifuge tube containing barium hydroxide solution was connected to the system, which was rapidly evacuated and then closed. Concentrated hydrochloric acid was released into the mixture, which was stirred for 1 hr. and warmed to 40° to assist diffusion of the liberated carbon dioxide. Barium carbonate (60 mg., 92%) was collected by centrifugation and the observed counting rate corrected for a 3% dilution with external carbon dioxide, as indicated by a blank reaction [Found: relative molar activity $\times 10^{-3}$, 57·8; 1*C requires 59·6].

Kuhn–Roth Oxidation of Orcinol.—Kuhn–Roth oxidation of orcinol (270 mg.) gave acetic acid, isolated by titration of the steam-distillate with 0·1N-lithium hydroxide. The *p*-bromophenacyl ester, m. p. 86° [from light petroleum (b. p. 40—60°)], was prepared for ^{14}C assay [Found: relative molar activity $\times 10^{-3}$, 62·2; 1*C requires 59·6], and the remainder of the lithium acetate degraded by pyrolysis *in vacuo* (cf. ref. 17) at 375—385° for 15 min. The residual lithium carbonate was converted into barium carbonate for counting [Found: relative molar activity $\times 10^{-3}$, 62·5; 1*C requires 59·6]. The acetone, condensed in a trap by cooling with liquid nitrogen, was oxidised with hypoiodite, and the iodoform sublimed at 110°/10 mm. before Van Slyke–Folch oxidation to barium carbonate [Found: relative molar activity, 0].

Decarboxylation of 3-Chloro-2-hydroxy-4 : 6-dimethoxybenzoic Acid.—An evacuated tube, containing the acid (65 mg.) beneath pre-heated glass wool, and connected to a centrifuge tube holding barium hydroxide solution, was immersed in a metal-bath at 270° for 5 min. After 20 min. the barium carbonate (54 mg., 98%) was collected and washed by centrifugation [Found: relative molar activity $\times 10^{-3}$, 61·0; 1*C requires 59·6].

The pyrolysis residue was collected with ether and sublimed at 80°/5 $\times 10^{-2}$ mm., to yield 2-chloro-3 : 5-dimethoxyphenol, m. p. 60—61° (42 mg., 81%) [Found: relative molar activity $\times 10^{-3}$, 176; 3*C requires 179].

Phloroglucinol from 3-Chloro-2-hydroxy-4 : 6-dimethoxybenzoic Acid.—2-Chloro-3 : 5-dimethoxyphenol, m. p. 60—61°, was prepared in 91% yield by heating the acid in a sealed tube at 260° for 7 min., and purified by sublimation at 80°/0·05 mm. The phenol (460 mg.), in 5% sodium hydroxide solution (35 ml.), was treated during 2 hr. with Raney nickel–aluminium alloy (2 g.) in small portions, with stirring. After a further hour, the nickel was filtered off and the filtrate poured into concentrated hydrochloric acid (20 ml.). Extraction with ether gave a viscous oil which sublimed at 80—100°/0·02 mm., and the phloroglucinol dimethyl ether (360 mg.) crystallised from benzene–light petroleum (b. p. 40—60°); it had m. p. 37—39° (lit.,[22] 36—38°).

Phloroglucinol dimethyl ether (360 mg.) was warmed for 70 min. on the water-bath with 5N-hydrochloric acid (11 ml.), the excess of acid neutralised with sodium carbonate, and the solution continuously extracted with ether to give a gum, which crystallised on the addition of benzene and sublimed at 190°/0·05 mm., yielding phloroglucinol (253 mg., 86%), m. p. 214—216° [Found: relative molar activity $\times 10^{-3}$, 175; 3*C requires 179].

2 : 4 : 6-*Trinitrophloroglucinol.*—Phloroglucinol (200 mg.) was nitrosated by the method of Freudenberg, Fikentscher, and Wenner [14] and the potassium salt oxidised, without isolation, by 30% hydrogen peroxide (1·5 ml.) (cf. ref. 15) after basification of the reaction mixture. After 2 hr., dilution with alcohol and filtration gave the yellow potassium salt of trinitrophloroglucinol (360 mg., 60%). Decomposition with dilute sulphuric acid gave trinitrophloroglucinol, yellow-orange needles, m. p. 160—161° (decomp.); Benedikt [23] records m. p. 158°.

Hypobromite Degradation of 2 : 4 : 6-Trinitrophloroglucinol.—To trinitrophloroglucinol (40 mg.) in water (4 ml.) at 0° was added a carbonate-free solution of barium hypobromite [from

[21] Cf. Calvin, Heidelberger, Reid, Tolbert, and Yankwich, "Isotopic Carbon," Wiley, New York, 1949, 92.
[22] Heilbron and Bunbury, "Dictionary of Organic Compounds," 1953, Vol. IV, p. 189.
[23] Benedikt, *Ber.*, 1878, **11**, 1374.

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barium hydroxide (1·6 g.) and bromine (0·22 ml.) in water (40 ml.)]. A centrifuge tube containing barium hydroxide solution was connected to the system, which was flushed with nitrogen and then closed. After 1 hour's stirring the system was evacuated and the mixture acidified with concentrated hydrochloric acid and warmed to 40°. The liberated carbon dioxide was collected as barium carbonate (66 mg., 72%) for counting [Found: relative molar activity × 10^{-3}, 61·7; 1*C requires 59·6]. The control value under these conditions was negligible.

The residual aqueous mixture was basified and the bromopicrin (112 mg., 82%) isolated and oxidised as before [Found: relative molar activity, 0].

Dechlorination of 3-Chloro-2-hydroxy-4 : 6-dimethoxybenzoic Acid.—Raney alloy (1·0 g.) was added during 1 hr. to the acid (179 mg.) in 5% sodium hydroxide solution (30 ml.) with stirring. After a further hour the nickel was filtered off and the filtrate poured into concentrated hydrochloric acid (20 ml.) with cooling. Filtration of the precipitate and sublimation at 150°/0·02 mm. gave 2-hydroxy-4 : 6-dimethoxybenzoic acid (140 mg., 92%), m. p. 155—157° (lit.,[24] 156°).

We are indebted to the Nuffield Foundation (Australia) for financial assistance in the early stages of this work, to C.S.I.R.O. for a Studentship (to R. W. R.), to the University of Manchester for a Science Research Scholarship (to R. A. M.-W.), and to Imperial Chemical Industries Limited for the loan of counting equipment.

THE UNIVERSITY, MANCHESTER, 13. [*Received, May 20th,* 1957.]

[24] Robertson, Suckling, and Whalley, *J.*, 1949, 1571.

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67. *Studies in Relation to Biosynthesis. Part XIV.* The Origin of the Nuclear Methyl Groups in Mycophenolic Acid.*

By A. J. BIRCH, R. J. ENGLISH, R. A. MASSY-WESTROPP, M. SLAYTOR, and HERCHEL SMITH.

Feeding experiments with [$^{14}CH_3$]methionine in the culture of *Penicillium brevi-compactum* have shown that the methoxyl and methyl groups attached to the benzene ring of the resulting mycophenolic acid (II; $R^1 = R^2 = H$, $R^3 = Me$) are derived from methionine.

STRUCTURAL comparisons led to the conclusion [1] that many natural products otherwise derived from acetic acid contain extra C_1 units (often methyl groups) introduced in a biosynthetic stage distinct from the formation of the main skeleton. The C_1-donors involved could be methionine, choline, or known carriers of formyl groups such as tetrahydrofolic acid, thus relating the process to the attachment of C_1 units to oxygen, nitrogen, or sulphur.[2] The nuclei to which attachment occurs are usually capable of high anionoid reactivity, notably in acylphloroglucinol or orcinol rings, and laboratory analogies for the postulated *C*-alkylations are available.[3] In some cases alkylation may occur in non-aromatic β-polyketone precursors.

A different hypothesis has been put forward [4] to explain the biosynthesis of the macrolides, which in our view are merely particular examples of the general type above. This postulates the intervention of propionic acid or an equivalent. To have any meaning in biochemical terms this amounts to postulating the introduction of C_3 units while the main skeleton is being formed. We recognise that this assumption explains very satisfactorily the structural relations in the macrolide field alone, particularly the presence in

* Part XIII, preceding paper.

[1] Birch, Elliott, and Penfold, *Austral. J. Chem.*, 1954, **7**, 169.
[2] Challenger, *Quart. Rev.*, 1955, **9**, 255.
[3] Riedl, *Annalen*, 1954, **585**, 38; Riedl and Risse, *ibid.*, p. 209.
[4] Flynn, Gerzon, Monahan, Quarck, Sigal, Weaver, and Wiley, *Chem. Eng. News*, 1956, **34**, 5138; Woodward, *Angew. Chem.*, 1957, **69**, 50.

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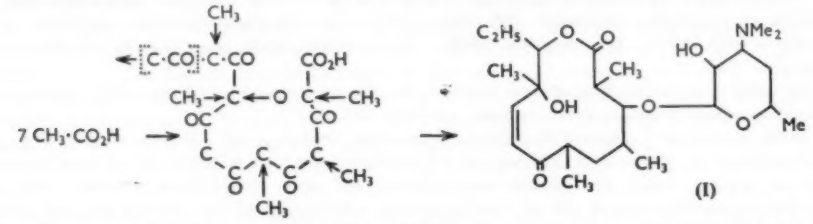
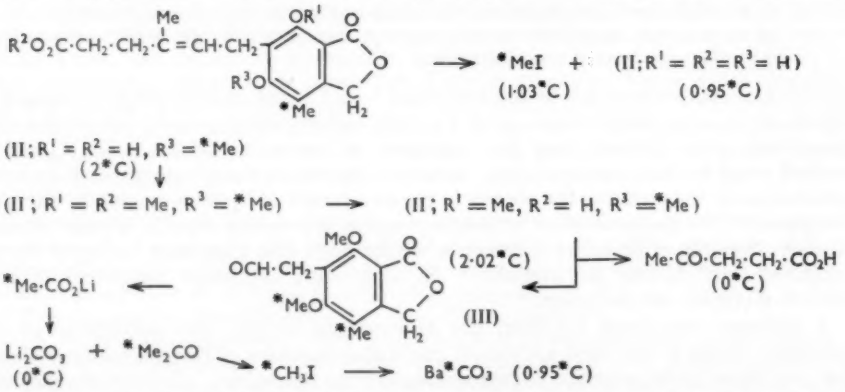
some cases of terminal ethyl groups. As a general hypothesis it has several unsatisfactory features, particularly the difficulty of including compounds containing *gem*-dimethyl or *iso*pentenyl or derived groups. Methymycin [5] (I) could arise as illustrated here.



(I)

To test whether the postulated *C*-methylation can occur we have examined the production of mycophenolic acid in *Penicillium brevi-compactum*. This substance is particularly suitable, being readily available and containing methoxyl, almost certainly derived from methionine, and an " extra " nuclear methyl group which can be compared with it: the rest of the molecule is entirely derivable from acetic acid.[6] The mould was grown in the presence of methionine containing $^{14}CH_3$. Labelled mycophenolic acid resulted with an astonishingly high incorporation (77%) of the added ^{14}C, and was degraded as shown in the chart. The results are expressed as in Part XIII; they leave no doubt that the hypothesis is correct in this case. The extent of labelling of the methoxyl is significantly higher than that of the nuclear methyl group. We attribute this to the presence of some unmethylated phenolic precursor at the stage of growth when methionine was introduced. The high utilisation of the latter indicates it is probably a limiting factor in synthesis. Mycophenolic acid grown on $Me\cdot{}^{14}CO_2H$ gave rise from the nucleus to $Me\cdot CO_2H$ which was, as expected, completely unlabelled.[6]

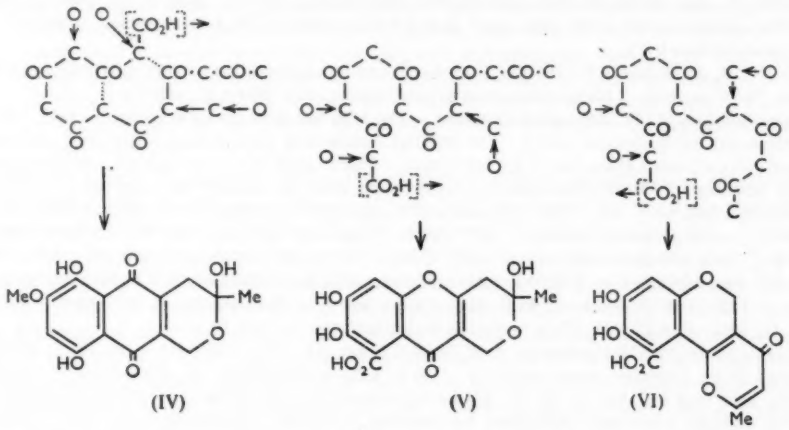
Many examples of the application of the theory could be cited. A most interesting series of mould metabolic products which can be structurally correlated are fusarubin (IV), fulvic acid (V), and citromycetin (VI). Despite superficial dissimilarities in the formulæ



all of these can be derived (on paper) from the same skeleton composed of seven acetic acid units with an introduced C_1 unit and two introduced oxygen atoms. It is significant that by changing the growth medium,[7] griseofulvin results instead of fulvic acid. This compound has been shown [8] to be derived from seven acetic acid units. For some reason the change of medium has apparently led to methylation on oxygen rather than on carbon.

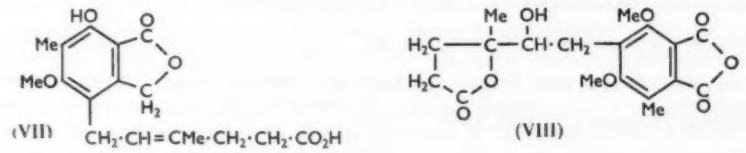
[5] Djerassi and Zderic, *J. Amer. Chem. Soc.*, 1956, **78**, 2907.
[6] Birch, English, Massy-Westropp, and Smith, following paper.
[7] Dean, Eade, Moubasher, and Robertson, *Nature*, 1957, **179**, 366.
[8] Birch, Massy-Westropp, Rickards, and Smith, *Proc. Chem. Soc.*, 1957, 98; preceding paper.

The Structure of Mycophenolic Acid.—When this work was begun one observation in the literature appeared to indicate preferentially the structure (VII) rather than (II; $R^1 = R^2 = H$, $R^3 = Me$) despite the very strong evidence presented for the latter.[9,10,11]



(IV) (V) (VI)

Oxidation of the methyl ether (II; $R^1 = R^3 = Me$, $R^2 = H$) by permanganate gave a substance formulated by Raistrick and his colleagues [9,10] as (VIII). After dissolution in hot ethanol it titrated as a monobasic acid and, after being heated in alkaline solution, as a tribasic acid. This behaviour was attributed to initial formation of an acid ethyl ester, which seemed to us unlikely in view of lack of reactivity with ethanol under similar conditions of other 2-alkyl-5-methoxyphthalic anhydrides which we have examined. Repetition of the oxidation and examination of the infrared spectrum shows, however, that (VIII) is correct. In chloroform solution no band is found attributable to a carboxyl group, but a hydroxyl is indicated by a broad band at 3550 cm.$^{-1}$. Strong bands at 1830, 1820, and 1760 cm.$^{-1}$ (broad) must be due to the anhydride ring (phthalic anhydride has bands at 1845 and 1775 cm.$^{-1}$). The expected absorption of the γ-lactone ring is probably included in the 1760 cm.$^{-1}$ band. Logan and Newbold [12] have proved structure (IX) by synthesis of a degradation product.



(VII) (VIII)

Experimental

Experimental directions are as for Part XIII. Where possible, substances were crystallised to constant specific activity.

[^{14}C]*Mycophenolic Acid.*—(*a*) *Penicillium brevi-compactum* was grown on standard Czapek-Dox medium at 25°.[13] After 27 days a solution of sodium [*carboxy*-^{14}C]acetate (0·5 mc) was

[9] Clutterbuck and Raistrick, *Biochem. J.*, 1933, **27**, 654.
[10] Birkinshaw, Bracken, Morgan, and Raistrick, *ibid.*, 1948, **43**, 216.
[11] Birkinshaw, Raistrick, and Ross, *ibid.*, 1952, **50**, 630.
[12] Logan and Newbold, *J.*, 1957, 1946.
[13] Clutterbuck, Oxford, Raistrick, and Smith, *Biochem. J.*, 1932, **26**, 1441.

added to three flasks, and growth continued for 14 days. The mould solution was filtered, acidified to pH 1 with hydrochloric acid, and extracted three times with ethyl acetate. The ethyl acetate extracts were dried and evaporated under reduced pressure at 35°. The residue was dissolved in absolute alcohol, and the potassium salt of mycophenolic acid isolated as described.[13] The residues were re-extracted three times, inactive acid being used as carrier, the total being diluted with pure acid (1·5 g.) and recrystallised to constant activity. The incorporation was 0·4%.

(*b*) [$^{14}CH_3$]Methionine [11] (165 mg.; 15·8 μc) was incorporated into mycophenolic acid as for sodium [1-^{14}C]acetate. Extraction gave mycophenolic acid (200 mg.; 12·2 μc).

Demethylation of [^{14}C]*Mycophenolic Acid.*—The acid (relative molar activity × 10^{-3}, 182) was demethylated by hydriodic acid.[9] The methyl iodide was collected at −20° and refluxed in ethanol (10 c.c.) with thiourea (1 g.) for 5 min. Picric acid (1 g.) was added and dissolved by further heating. *S*-Methylthiuronium picrate separated on cooling and after recrystallisation from alcohol had m. p. 223—224° (Brown and Campbell [15] give 224°) (Found: C, 30·2; H, 2·6; N, 21·2%; relative molar activity × 10^{-3}, 93·8. Calc. for $C_8H_9N_5O_7S$,1*C: C, 30·0; H, 2·8; N, 21·8%; relative molar activity × 10^{-3}, 91·0). The normycophenolic acid (II; $R^1 = R^2 = R^3 = H$) was sublimed at 158°/0·1 mm. and recrystallised from benzene–light petroleum. It had m. p. 183—184° (Found: C, 62·6; H, 5·8%; relative molar activity × 10^{-3}, 86·6. Calc. for $C_{16}H_{18}O_6$,1*C: C, 62·7; H, 5·9%; relative molar activity × 10^{-3}, 91·0).

Ozonolysis of [^{14}C]*Mycophenolic Acid Methyl Ether* (II; R^1 = Me, R^2 = H, $R^3 = {}^{14}CH_3$).—The acid (1 g.) (relative molar activity × 10^{-3}, 153) was ozonised in chloroform [10] (150 c.c.). Lævulic acid was isolated as the 2 : 4-dinitrophenylhydrazone which, after precipitation from aqueous sodium hydrogen carbonate by mineral acid and recrystallisation from methanol, had m. p. 204—205° (Found: C, 44·8; H, 3·9%; relative molar activity, 0. Calc. for $C_{11}H_{12}O_6N_4$: C, 44·6; H, 4·0%). The phenylacetaldehyde derivative also produced was obtained as the 2 : 4-dinitrophenylhydrazone which was purified by chromatography on bentonite (18 g.)–kieselguhr (6 g.) in 3 : 97 ethanol–chloroform and, after recrystallisation from methanol, had m. p. 213—214° (Found: C, 53·2; H, 4·3%; relative molar activity × 10^{-3}, 154. Calc. for $C_{15}H_{16}O_8N_4$,2*C: C, 53·0; H, 4·2%; relative molar activity × 10^{-3}, 153). The above 2 : 4-dinitrophenylhydrazone was oxidised by the Kuhn–Roth method. The resulting acetic acid was isolated as lithium acetate which was heated *in vacuo* at 500° for 10 min. to give lithium carbonate and acetone (cf. ref. 8). The former was converted into barium carbonate for radioactive assay (Found: relative molar activity, 0). The latter was treated with hypoiodite to give iodoform, Van Slyke–Folch oxidation of which gave further barium carbonate for counting (Found: relative molar activity × 10^{-3}, 71·6; 1*C requires 76·5).

Grants from the Nuffield Foundation (Australia) (to M. S.) and from the Cumberland Education Committee (to R. J. E.) are gratefully acknowledged. We also thank the University of Manchester for the award of a Science Research Scholarship (to R. M.-W.) and Imperial Chemical Industries Limited for the loan of counting equipment.

UNIVERSITY OF MANCHESTER, MANCHESTER, 13. [*Received, June 21st*, 1957.]

[14] Calvin, Heidelberger, Reid, Tolbert, and Yankwich, "Isotopic Carbon," Wiley, New York, 1949, p. 222.
[15] Brown and Campbell, *J.*, 1937, 1699.

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68. *Studies in Relation to Biosynthesis. Part XV.* Origin of Terpenoid Structures in Mycelianamide and Mycophenolic Acid.*

By A. J. Birch, R. J. English, R. A. Massy-Westropp, and Herchel Smith.

Incorporations of [*carboxy*-^{14}C]acetic acid, 3-methyl[1-^{14}C]but-2-enoic acid, and βδ-dihydroxy-β-methyl[α-^{14}C]valeric (mevalonic) lactone into the terpenoid chains of mycelianamide (II) and mycophenolic acid (XVI) have been examined and compared in the first case with the incorporation into griseofulvin (IX) and in the second case with the incorporation into the acetic acid-derived portion of the molecule. The biogenesis of *iso*pentane units is discussed.

The way in which the methyl- and carboxyl-carbon atoms of acetic acid contribute to the *iso*pentane unit in natural compounds was first elucidated by work on steroid biosynthesis.[1] In 1952 one of us independently advanced [2] the same pattern (I). The active intermediate in mind at the time was 3-methylglutaconic acid. Work was begun in conjunction with A. R. Penfold and J. L. Willis (Museum of Applied Arts and Sciences, Sydney) to examine the mode of incorporation of [*carboxy*-^{14}C]acetic acid into the citronellal of the essential oil of *Eucalyptus citriodora* Hook but failed owing to insufficient incorporation of the tracer. Our joint views were set out in a lecture.[3] Much experimental evidence has accumulated during the last five years in the fields of carotenoids,[4] steroids,[1] and triterpenes [5] that the pattern (I) is correct. However, intermediate stages between C_2 and C_5 compounds still require investigation.

We sought mould metabolic products containing simple terpenoid chains for study with isotopically labelled compounds. Two suitable substances appeared to be mycelianamide [6,7] (II) containing a C_{10} terpenoid chain readily isolated as methylgeraniolene (III) by reduction with sodium and liquid ammonia,[7] and mycophenolic acid [8] (XIV), the C_7 side-chain of which we regard as the remnant of an oxidised geranyl group.

Mycelianamide.—Mycelianamide is produced by *Penicillium griseofulvum* Dierckx (L.S.H. Cat. No. P. 38) simultaneously with griseofulvin (VIII) which previous studies [9] have shown to be directly derived from acetic acid. This mould therefore provides an opportunity to study the relative effectiveness of various sources for the production of an isoprenoid chain and of a substance directly formed from acetic acid. The two compounds are produced by the mould in approximately constant ratio throughout its growth and so the extent of incorporation into griseofulvin is a measure of the biochemical conversion of the added labelled compound into acetic acid.

Addition of Me·$^{14}CO_2H$ gave rise to labelled mycelianamide and griseofulvin. The degradation of the former was carried out as below, the results being set out as in our previous work.[9] It can be seen that they agree quantitatively with the expected distribution (II). The efficiency of incorporation of acetic acid is of the same order in both cases.

Addition to the mould of $Me_2C{:}CH{\cdot}{}^{14}CO_2H$, another possible source of *iso*pentane units, also gave rise to mycelianamide with the distribution of ^{14}C found in (II), as shown by the annexed degradations. The griseofulvin simultaneously produced has the activity to be

* Part XIV, preceding paper.

[1] For reviews see Cornforth, *Rev. Pure Appl. Chem.* (*Australia*), **1954**, **4**, 275; Friedman, Byers, and St. George, *Ann. Rev. Biochem.*, **1956**, **25**, 613; cf. Cornforth, Gore, and Popjak, *Biochem. J.*, **1956**, **25**, 613, and earlier papers.

[2] Birch, *Perfumery Essent. Oil Record*, 1952, **43**, 110.

[3] Penfold, *Perfumery Essent. Oil Record*, 1954, **45**, 213.

[4] *Inter al.*, Reichel and Wallis, *Naturwiss.*, 1957, **44**, 234; Grob and Bütler, *Experientia*, 1955, **7**, 259.

[5] Dauben and Richards, *J. Amer. Chem. Soc.*, 1956, **78**, 5329.

[6] Oxford and Raistrick, *Biochem. J.*, 1948, **42**, 323.

[7] Birch, Massy-Westropp, and Rickards, *J.*, 1956, 3717.

[8] Birkinshaw, Raistrick, and Ross, *Biochem. J.*, 1952, **50**, 630.

[9] Birch, Massy-Westropp, Rickards, and Smith, *Proc. Chem. Soc.*, 1957, 98; *J.*, 1957, 360.

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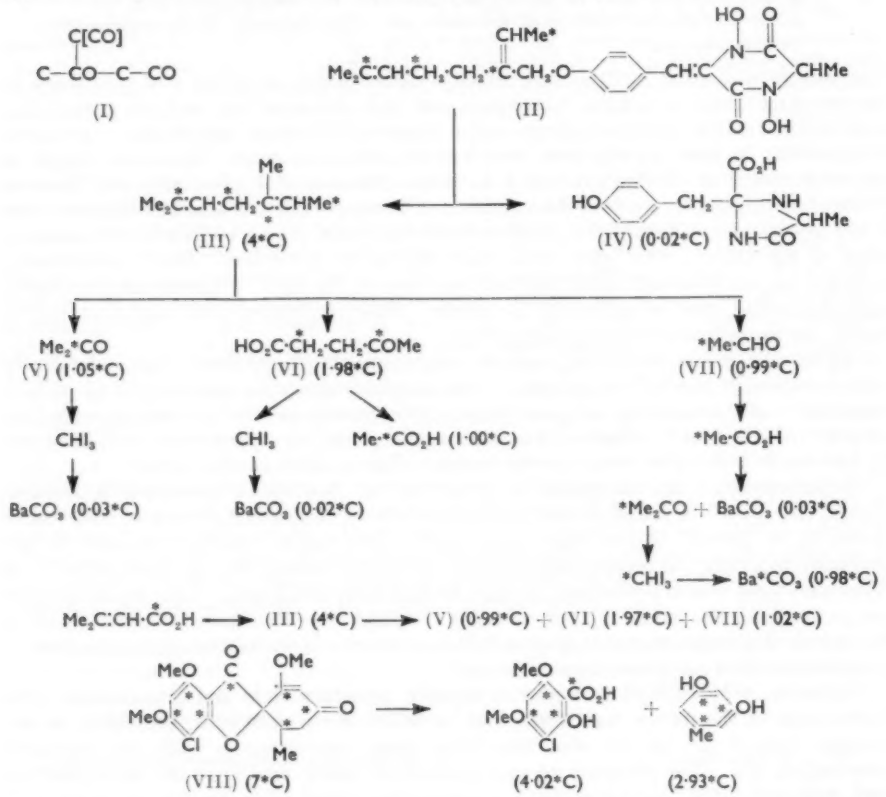
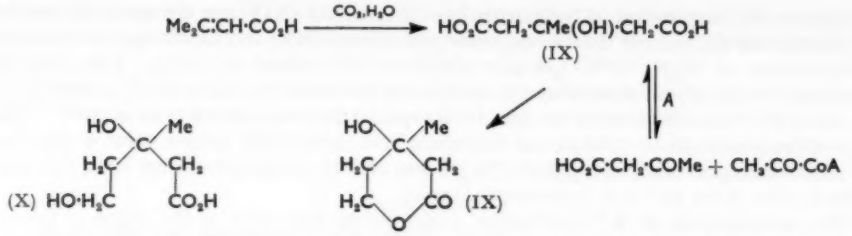
predicted on the basis of its formation from $Me\cdot{}^{14}CO_2H$ of the same degree of labelling as that giving rise to the mycelianamide. To confirm that the distribution of labelling in the griseofulvin is the same as that already observed,[9] hydrolytic fission was carried out by Mr. R. W. Rickards and the resulting orcinol and 3-chloro-2-hydroxy-4 : 6-dimethoxybenzoic acid shown to have the calculated activities. These results are conclusive in showing that the $Me_2C{:}CH\cdot{}^{14}CO_2H$ is not incorporated as a unit, but undergoes degradation to acetic acid before incorporation. The equilibrium *A* must therefore be set up, in this organism at least, far more rapidly than the β-hydroxy-β-methylglutaric acid



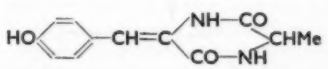
(IX) is converted into the direct *iso*pentane precursor, probably mevalonic acid[10] (X). In contrast to these results Bloch, Clarke, and Harary[11] reported the incorporation of $Me_2C{:}CH\cdot{}^{14}CO_2H$ *en bloc* into cholesterol in rats, and Sanderman and Stockman[12] made similar observations on the biosynthesis of pulegone in *Mentha pulegium* L.

A study of the incorporation of [2-^{14}C]mevalonic lactone (XI) reveals that this substance is indeed an irreversible intermediate in terpene biosynthesis, no longer giving rise to labelled acetic acid. The degradations of the resulting methylgeraniolene shown on p. 371 support the distribution (XII). It is particularly notable that the labelled carbon atom at position 4 is not interchanged with that in the 3-methyl group. This should be important when tracing biosynthetic routes in terpenoid compounds with complex ring

[10] Wolf, Hoffman, Aldrich, Skeggs, Wright, and Folkers, *J. Amer. Chem. Soc.*, 1956, **78**, 4497; 1957, **79**, 1486.
[11] Bloch, Clarke, and Harary, *ibid.*, 1954, **76**, 3859.
[12] Sanderman and Stockman, *Naturwiss.*, 1956, **43**, 580.

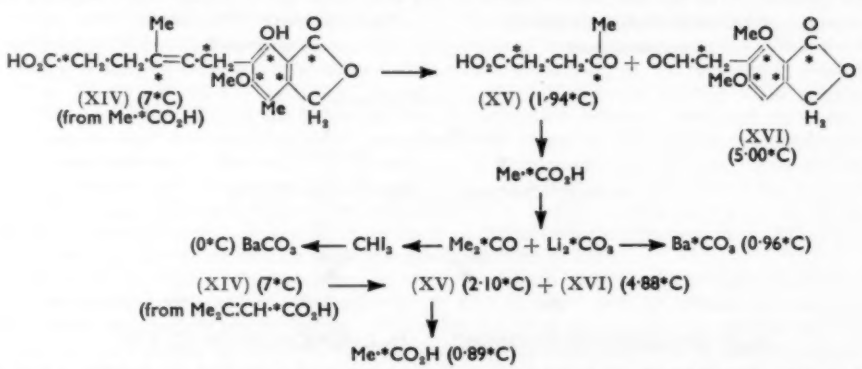


systems. The griseofulvin produced simultaneously is completely inactive, indicating the complete absence of $^{14}CH_3 \cdot CO_2H$.



Reduction of mycelianamide with sodium and methanol in liquid ammonia gives, in addition to methylgeraniolene, a substance $C_{13}H_{14}O_4N_2$ which is soluble in aqueous sodium hydrogen carbonate, insoluble in mineral acid, and fails to react with nitrous acid. It is a carboxylic acid (infrared spectrum) and on acid hydrolysis gives *p*-hydroxyphenylpyruvic acid. Its light absorption is similar to that of *p*-ethylphenol [13] and it is therefore formulated as the tetrahydroglyoxaline derivative (IV), presumably formed by hydrolysis and recyclisation of the initially formed piperazine (XIII).

Mycophenolic Acid.—With this substance (XIV) we are able, as will be shown, to study the incorporation of precursors into an isoprenoid chain and an acetic acid-derived nucleus

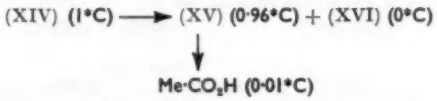


in the same molecule. The degradations below establish that $Me \cdot {}^{14}CO_2H$ produces the expected labelling pattern (XIV) and it is notable that the extent of incorporation into the nucleus and into the side chain is exactly the same. The results obtained with mycelianamide from $Me_2C{:}CH \cdot {}^{14}CO_2H$ are substantially confirmed, in that the labelling pattern is closely similar to that produced directly from $Me \cdot {}^{14}CO_2H$. It will be noted that the activities of the lævulic acid (XV) and the aldehyde (XVI) are respectively higher (by 5%) and lower (by 2·5%) than the values predicted for complete derivation from $Me \cdot {}^{14}CO_2H$. We regard these variations as indicating some incorporation of $Me_2C{:}CH \cdot {}^{14}CO_2H$ as a unit into (XIV). If it is assumed that $Me_2C{:}CH \cdot {}^{14}CO_2H$ gives rise as above to $Me \cdot {}^{14}CO_2H$ with one-third of the original specific molar activity, and that the

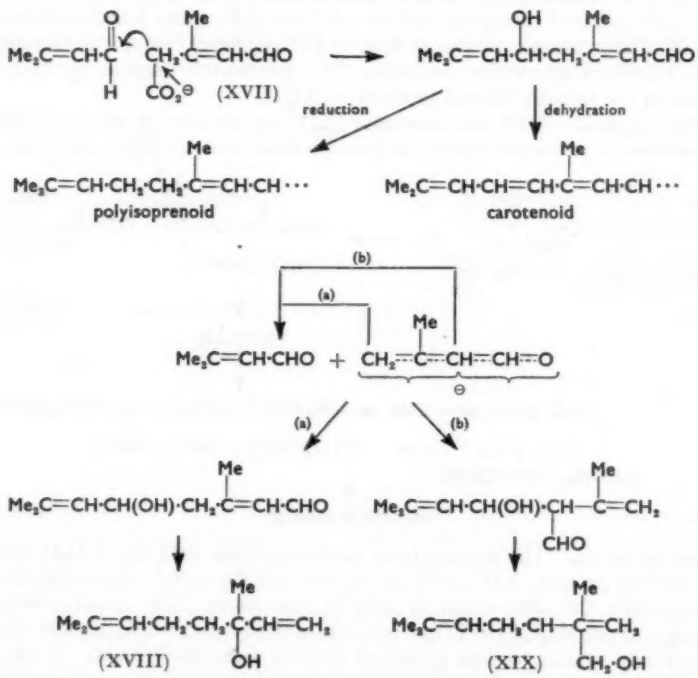
[13] Friedel and Orchin, "Ultraviolet Spectra of Aromatic Compounds," Wiley and Sons Inc., New York, 1951, p. 37.

efficiencies of incorporation of both acids into the product (XIV) are the same, it may be calculated that the ratio of the specific molar activities of (XV) and (XVI) represents direct incorporation of $Me_2C{:}CH{\cdot}{}^{14}CO_2H$ into (XIV) to the extent of 7·5%. This view is reinforced by the observation that the acetic acid obtained by Kuhn–Roth oxidation of the acid (XV) has a lower activity than that required for biosynthesis from acetate. The ratio of the specific molar activities of this acetic acid and of (XV) gives a value of 11% for the direct incorporation of $Me_2C{:}CH{\cdot}{}^{14}CO_2H$ into (XIV), in fair agreement with the first value in view of the probable experimental errors.

The incorporation of [2-^{14}C]mevalonic acid confirms our view on the origin of the C_7 chain, because the nucleus is then completely unlabelled, and all of the labelling is present in the lævulic acid produced by ozonolysis. Proof is again provided that mevalonic acid is a specific intermediate in terpene biosynthesis.



The mode of incorporation of the C_6 compound mevalonic acid into substances containing the C_5 *iso*pentane unit involves decarboxylation.[14] We believe that the process may involve initial oxidation to the aldehyde-acid (XVII), decarboxylation of which, as its



anion, will be facilitated by its structure as a " vinylogue " of a β-aldehydo-acid. The resulting anion could then react with the carbonyl group of another similar unit, with later further decarboxylation, or with β-methylcrotonaldehyde produced by proton-addition to the anion. An advantage of this view is that the process can continue indefinitely, since the necessary activation is supplied by the unit added to the end of the chain. The

[14] Tavormina, Gibbs, and Huff, *J. Amer. Chem. Soc.*, 1956, **78**, 4498.

intermediate alcohol could be dehydrated to give conjugated polyenes of the carotenoid type, or hydrogenolysed to polyisoprenes, possibly by the kind of process postulated [15] for hydrogenolysis of some natural allyl alcohol derivatives.

The head-to-head or tail-to-tail linkage of *iso*pentane units which appears to occur in some compounds is explicable on the basis of migrations, usually of methyl groups. An interesting case whose significance has already been noted [3] is the co-occurrence of linaloöl (XVIII) and lavendulol (XIX) where the relationship could be as illustrated.

Experimental

General directions are as in the two preceding papers.

[^{14}C]*Mycelianamide and* [^{14}C]*Griseofulvin.*—(*a*) *Penicillium griseofulvum* Dierckx (L.S.H. Catalogue No. P. 38) was cultured under the conditions described previously.[6] After 18 days a solution of sodium [*carboxy*-^{14}C]acetate (1·0 mc; 7·6 mg.) was distributed among 8 flasks, each containing 350 ml. of medium. After a further 9 days at 30°, [^{14}C]mycelianamide (1·2 g.), m. p. 168—170° (decomp.), and griseofulvin (0·2 g.), m. p. 219—220°, were isolated. An aliquot part (900 mg.) of the impure mycelianamide was diluted with pure, inactive mycelianamide (17·5 g.) and on recrystallisation from ethanol had m. p. 171—172° (decomp.). The incorporation of tracer into mycelianamide and griseofulvin was about 2% and 1% respectively.

(*b*) The mould was grown as above, except that 3-methyl[1-^{14}C]but-2-enoic acid (136 μc) was added in place of sodium [*carboxy*-^{14}C]acetate. Mycelianamide (800 mg., 0·71%; 0·96 μc) and griseofulvin (210 mg., 0·41%; 0·56 μc) were obtained. The ratio of the molar specific activities is 7·2 : 4; biosynthesis from Me·$^{14}CO_2Na$ of the same activity requires a theoretical ratio 7 : 4. Both metabolites were diluted before degradation.

(*c*) The mould was grown with βδ-dihydroxy-β-methyl[α-^{14}C]valeric lactone [16] (42·8 μc). Radioactive mycelianamide (0·34 μc; 0·79%) was obtained; the incorporation of tracer into the griseofulvin was insignificant.

Reduction of [^{14}C]*Mycelianamide.*—Mycelianamide (14·8 g.) was reduced with sodium and methanol in liquid ammonia as previously described,[7] to give methylgeraniolene (3·22 g., 62%). The solution, after removal of the latter, was kept at room temperature for 48 hr., filtered, and acidified with concentrated hydrochloric acid. The precipitate was dissolved in aqueous potassium hydrogen carbonate solution and recrystallised from ethanol, to give *tetrahydro*-2-(*4-hydroxybenzyl*)-*5-methyl*-*4-oxoglyoxaline*-*2-carboxylic acid* (XIV), m. p. 285—288° (Found: C, 57·4; H, 5·7; N, 11·8. $C_{13}H_{14}O_4N_2$ requires C, 57·6; H, 5·6; N, 11·2%). The infrared absorption spectrum (Nujol mull) showed broad absorption between 3400 and 2500 cm.$^{-1}$ (hydrogen-bonded carboxylic-hydroxyl stretching) and bands at 1697 (carboxylic-carbonyl), 1657 (amide-carbonyl), 1610 and 1525 (aromatic C=C stretching) and 830 cm.$^{-1}$ (out-of-plane C–H deformation in 1 : 4-disubstituted benzene ring). In EtOH $\lambda_{max.}$ 226 and 277 mμ (ε 10,500 and 2000); $\lambda_{min.}$ 252 mμ (ε 910). The acid (XIV) with 2N-hydrochloric acid gave, in 13 hr., *p*-hydroxyphenylpyruvic acid identified as the 2 : 4-dinitrophenylhydrazone, m. p. 169—171°, undepressed by admixture with an authentic specimen of m. p. 173°.

Ozonolysis of [^{14}C]*Methylgeraniolene.*—(i) Ozonised oxygen was passed through a solution of methylgeraniolene (600 mg.) in ethyl chloride (15 c.c.) at −30° until the effluent gas liberated iodine from aqueous potassium iodide. Water (10 c.c.) was added and the solution refluxed for 30 min. in a stream of nitrogen, the emerging vapours being collected in Brady's reagent, to give a mixture of acetone and acetaldehyde 2 : 4-dinitrophenylhydrazones. A solution of potassium dichromate (2·85 g.) in water (30 ml.) and concentrated sulphuric acid (3·75 g.) was added to the residual mixture, the whole being kept for 3 hr. at room temperature, whereafter water (300 ml.) was added. Continuous ether-extraction gave lævulic acid obtained as the 2 : 4-dinitrophenylhydrazone, m. p. 206°. Chromatography of the mixture of acetone and acetaldehyde 2 : 4-dinitrophenylhydrazones on bentonite (21 g.) and kieselguhr (7 g.) in ether–ethanol gave acetone and acetaldehyde 2 : 4-dinitrophenylhydrazones, m. p. 127° and 169° respectively.

(ii) Methylgeraniolene (324 mg.) was ozonised in sulphur-free light petroleum (10 c.c.; b. p. 60—80°) at 0°. Acetic acid (2 c.c.) was added, the light petroleum distilled off, and the residue shaken for 1 hr. at room temperature with 30% hydrogen peroxide (0·5 c.c.). Water (3 c.c.) and more 30% hydrogen peroxide (2 c.c.) were added and the mixture was heated for 3 hr. at

[15] Birch and Slaytor, *Chem. and Ind.*, 1956, 1524.

[16] Cornforth, Cornforth, and Youhotsky-Gore, *Biochem. J.*, 1957, **66**, 10P.

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70°. The solution was brought to pH 5 with N-sodium hydroxide and steam-distilled. The distillate contained acetone (obtained as the 2 : 4-dinitrophenylhydrazone); a portion was oxidised with aqueous sodium hypoiodite to iodoform (70 mg.) which was recrystallised from methanol and oxidised by the Van Slyke–Folch procedure to barium carbonate. The residual solution from the steam-distillation was continuously extracted with ether, to give lævulic acid, oxidation of which with alkaline hypoiodite solution gave iodoform converted, as before, into barium carbonate. Kuhn–Roth oxidation of the above acetaldehyde 2 : 4-dinitrophenylhydrazone gave acetic acid, isolated as lithium acetate, pyrolysis of which *in vacuo* at 380° for 15 min. gave acetone and a residue of lithium carbonate. This salt was converted into barium carbonate. Alkaline hypoiodite treatment of the acetone gave iodoform, converted, as above, into barium carbonate.

[^{14}C]*Mycophenolic Acid.*—(*a*) Sodium [*carboxy*-^{14}C]*acetate* was incorporated to the extent of 0·4% into mycophenolic acid produced by *Penicillium brevi-compactum* Dierckx as described in Part XIV.

(*b*) Addition of 3-methyl[1-^{14}C]but-2-enoic acid (136 μc) to the culture medium gave mycophenolic acid (0·66 μc; 0·49%).

(*c*) Addition of ββ-dihydroxy-β-methyl[α-^{14}C]valeric lactone (20·7 μc) to the culture medium gave mycophenolic acid (0·31 μc; 1·5%). The degradations of labelled mycophenolic acid were carried out as described in Part XIV.

Radioactive Assay.—The results of the radioactive assay of the degradation products of various samples of mycelianamide, griseofulvin, and mycophenolic acid are given in the following Tables. Acetone, lævulic acid, acetaldehyde, and the aldehyde (XVI) were assayed as the 2 : 4-dinitrophenylhydrazones, acetic acid as the *p*-bromophenacyl ester.

Substance	Relative molar activities ($\times 10^{-3}$) Found	Required
Mycelianamide (II) from Me·$^{14}CO_2H$	457	—
2-(4′-Hydroxybenzyl)-5-methyl-4-oxoglyoxaline-2-carboxylic acid (IV)	3	—
Methylgeraniolene (III)	454 (by diff.)	—
Acetone (V) from (III)	119	113
Barium carbonate *ex* iodoform from (V)	3	0
Lævulic acid (VI) from (III)	225	227
Barium carbonate *ex* iodoform from (VI)	2	0
Acetic acid from (VI)	113	113
Acetaldehyde (VII)	112	113
Ba carbonate *ex* acetic acid from (VII)	3	0
Ba carbonate *ex* iodoform from acetone from (VII)	111	113
Mycelianamide from $Me_2C{:}CH{\cdot}^{14}CO_2H$	69·2	—
Methylgeraniolene	67·8	—
Acetone	16·9	17·0
Lævulic acid	33·3	33·9
Acetaldehyde	17·3	17·0
Griseofulvin (VIII) from $Me_2C{:}CH{\cdot}^{14}CO_2H$	164	—
3-Chloro-2-hydroxy-4 : 6-dimethoxybenzoic acid	94·2	93·6
Orcinol	68·6	70·2
Methylgeraniolene (XII) from lactone of [2-^{14}C]mevalonic acid	33·4	—
Acetone from (XII)	16·5	16·7
Lævulic acid from (XII)	17·1	16·7
Acetaldehyde from (XII)	0·7	0
Mycophenolic acid (XIV) from Me·$^{14}CO_2H$	212	—
Aldehyde (XVI)	152	152
Lævulic acid (XV) from (XIV)	58·9	60·6
Ba carbonate *ex* acetic acid from (XV)	29·1	30·3
Ba carbonate *ex* iodoform from acetone from above acetic acid	0	0
Mycophenolic acid from $Me_2C{:}CH{\cdot}^{14}CO_2H$	86·4	—
Aldehyde (XVI)	60·2	61·7
Lævulic acid (XV)	25·9	24·7
Acetic acid	11·0	12·4
Mycophenolic acid (XIV) from mevalonic lactone	65·1	—
Aldehyde (XVI)	0	0
Lævulic acid (XV)	62·5	65·1
Acetic acid from lævulic acid	0·9	0

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We thank the University of Manchester for a Science Research Scholarship (to R. A. M.-W.), the Cumberland Education Committee for a grant (to R. J. E.), Dr. R. H. Cornforth (Mill Hill) and Mr. J. Schofield for synthesis of the labelled valerolactone and methylbutenoic acid respectively, and Miss M. Hay for mycological work. Counting equipment was kindly lent by Imperial Chemical Industries Limited.

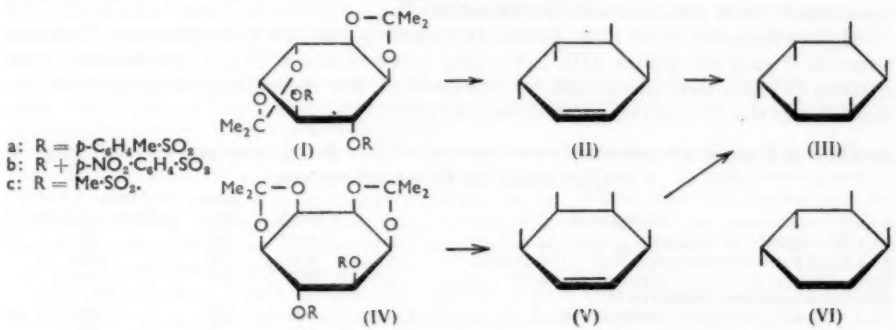
UNIVERSITY OF MANCHESTER, MANCHESTER, 13. [*Received, August 1st*, 1957.]

69. *Cyclitols. Part VIII.* Elimination of Vicinal Sulphonyloxy-groups by Iodide Ion.*

By S. J. ANGYAL and P. T. GILHAM.

Two *cyclo*hex-5-ene-1 : 2 : 3 : 4-tetrols (II) and (V) were prepared by elimination of two secondary sulphonyloxy-groups by iodide ion from suitably substituted inositols. The *p*-nitrobenzenesulphonyloxy-group is more readily eliminated than the toluene-*p*-sulphonyloxy-group.

IN an attempt to synthesise *cis*inositol, the all-*cis*-*cyclo*hex-5-ene-1 : 2 : 3 : 4-tetrol (V) was prepared; it was hoped that its *cis*-hydroxylation would yield some *cis*inositol. However, addition occurred from the unhindered side and *allo*inositol (III) was the only product; *cis*inositol was subsequently obtained by a different route.[1] Preparation of the unsaturated tetrol, and of a diastereomer, is now described.



The preparations involved elimination of two vicinal sulphonyloxy-groups by iodide ion, which has several times been used in the carbohydrate field [2] but is there applicable only to compounds in which one of the sulphonyloxy-groups is primary. There is one case [3] of the formation of iodine and sodium toluene-*p*-sulphonate from a sugar derivative containing two secondary toluene-*p*-sulphonyl groups, but there no other product could be isolated. Elimination of secondary sulphonyloxy-groups is possible, however, from some other type of compounds, such as steroids [4] and αβ-diacyloxy-carboxylic acids.[5]

The readily available di-*O*-*iso*propylidene derivative (Ia) of 3 : 4-di-*O*-tosyl-(−)-inositol [6] † was used for the first experiments. Both toluene-*p*-sulphonyloxy-groups,

* Part VII, *J.*, 1957, 3691.

† For the pair of optically active inositols, (+)- and (−)- take the place of prefixes. In this paper these symbols, placed *immediately* before "inositol," denote the configurational series and not necessarily the sign of rotation of the complete compound. [N.B. This practice must not be generalised, as it is contrary to I.U.P.A.C. rules (see *J.*, 1951, 3522). ED.] The modified (*R*)(*S*) nomenclature [7] is used in the experimental section.

[1] Angyal and McHugh, *J.*, 1957, 3682.
[2] For a summary, see Tipson, *Adv. Carbohydrate Chem.*, 1953, **8**, 201.
[3] Owen and Bladon, *J.*, 1950, 598.
[4] Slates and Wendler, *Chem. and Ind.*, 1955, 168; *J. Amer. Chem. Soc.*, 1956, **78**, 3749.
[5] Linstead, Owen, and Webb, *J.*, 1953, 1220.
[6] Angyal and Matheson, *J. Amer. Chem. Soc.*, 1955, **77**, 4343.

although secondary, reacted smoothly with sodium iodide in acetone; reaction was nearly complete in 24 hours at 100° or in 2 hours at 140° and gave (+)-*cyclo*hex-5-ene-1 : 2/3 : 4-tetrol (II) as its di*iso*propylidene derivative. Hydrolysis gave the free tetrol. Di-*O*-tosyl-(−)-inositol itself also reacted with sodium iodide but its tetra-acetate did not, even at 140°, probably owing to steric hindrance. These and other runs are summarised in the Table.

However, the di-*O-iso*propylidene derivative (IVa) of 5 : 6-di-*O*-tosyl*epi*inositol [7] did not react with sodium iodide at 100° and even at 140° the reaction required long heating, with consequent destruction of the unsaturated tetrol (V) presumably formed. The di-*O-iso*propylidene derivative (Ib) of 3 : 4-di-*O-p*-nitrobenzenesulphonyl-(−)-inositol underwent elimination faster than the toluene-*p*-sulphonyl analogue, in accord with a suggestion by Tipson.[8] The di-*O-iso*propylidene derivative (IVb) of 5 : 6-di-*O-p*-nitrobenzenesulphonyl*epi*inositol was sufficiently reactive at 100° to allow the preparation of the di-*O-iso*propylidene derivative of the all-*cis-cyclo*hex-5-ene-1 : 2 : 3 : 4-tetrol (V). Even the tetra-acetate of the dinitrobenzenesulphonyl compound reacted in boiling acetic anhydride with sodium iodide, giving the tetra-acetate of (V). The free tetrol (V) itself, however, could not be obtained crystalline.

The di-*O-iso*propylidene derivative (Ic) of 3 : 4-di-*O*-methanesulphonyl-(−)-inositol, prepared in the hope that the smaller sulphonyloxy-groups would prove more reactive, showed surprisingly low reactivity with sodium iodide (see Table).

The mechanism of the elimination, which is not clearly understood despite some recent discussion,[3,9] is at present under investigation.

Hydroxylation of the 1 : 2/3 : 4-tetrol (II) by silver chlorate in the presence of osmium tetroxide [10] gave *allo*inositol (III),[11] providing a new synthesis of this rare inositol. The *cis*tetrol (V) also gave *allo*inositol by this reaction, but the other possible product, *cis*-inositol, was not detected by paper chromatography.

Reaction of disulphonyl compounds with sodium iodide. (0·5 g. of compound and 1·5 g. of sodium iodide in 10 ml. of acetone.)

Compound	Temp.	Time (hr.)	Yield (%) of sodium sulphonate
3 : 4-Di-*O*-tosyl-(−)-inositol	100°	20	85
3 : 4-Di-*O-p*-nitrobenzenesulphonyl-(−)-inositol	100	10	100
Tetra-*O*-acetyl-3 : 4-di-*O*-tosyl-(−)-inositol *	140	13	0
Di-*O-iso*propylidene derivative of:			
3 : 4-di-*O*-tosyl-(−)-isositol (Ia)	100	23	99
	140	2	81
3 : 4-di-*O-p*-nitrobenzenesulphonyl-(−)-inositol (Ib)	100	13	93
3 : 4-di-*O*-methanesulphonyl-(−)-inositol (Ic)	100	20	9
5 : 6-di-*O*-tosyl*epi*inositol (IVa)	100	20	0
	140	10	95
5 : 6-di-*O-p*-nitrobenzenesulphonyl*epi*inositol (IVb)	100	20	69

* 0·3 g. of sodium iodide.

Hydrogenation of the tetrol (II) gave (+)-*cyclo*hexane-1 : 2/3 : 4-tetrol (VI), $[\alpha]_D^{26}$ +72° (in H_2O). Posternak and Friedli [10] prepared the racemic form of this compound by the hydroxylation of (±)-*cis-cyclo*hex-3-ene-1 : 2-diol and resolved it by the action of *Acetobacter suboxydans* which dehydrogenated only one enantiomorph. The unattacked stereoisomer, the configuration of which was not known to the Swiss workers, had a rotation of −74° and was therefore the enantiomer of our compound, the action of *A. suboxydans* being in agreement with the rules proposed by Magasanik, Franzl, and Chargaff.[12]

In an attempt to prepare cyclitols by cyclisation, Micheel [13] treated what he believed

[7] Angyal and Gilham, *J.*, 1957, 3691.
[8] Ref. 2, p. 211.
[9] Foster and Overend, *J.*, 1951, 3452; Newth, *J.*, 1956, 471.
[10] Posternak and Friedli, *Helv. Chim. Acta*, 1953, **36**, 251.
[11] Dangschat and Fischer, *Naturwiss.*, 1939, **27**, 756.
[12] Magasanik, Franzl, and Chargaff, *J. Amer. Chem. Soc.*, 1952, **74**, 2618
[13] Michael, *Annalen*, 1932, **496**, 96.

to be 1 : 6-dideoxy-1 : 6-di-iodo-2 : 3-4 : 5-dimethylene-D-mannitol with "molecular" silver at 165—170° and obtained, after hydrolysis of the methylene groups, a compound to which he ascribed structure (VI). The properties of his compound are different, however, from those of ours or of its enantiomorph, indeed from those of any *cyclo*hexane-1 : 2 : 3 : 4-tetrol, all of which are now known.[14] It is also clear now[15] that Micheel's starting material had the methylene groups in the 2 : 4-3 : 5-positions (not 2 : 3-4 : 5) which would make cyclisation to a six-membered ring sterically impossible without inversion or rearrangement. The structure and configuration of Micheel's compound are therefore unknown.

Experimental

M. p.s are corrected. Analyses are by Dr. E. Challen and Mr. D. G. Weeden.

(1R)-1 : 2 : 5 : 6-*Tetra*-O-*acetyl*-3 : 4-*di*-O-*tosylinositol*.—(1*R*)-3 : 4-Di-*O*-tosylinositol[6] (0·5 g.) was heated for 1 hr. at 100° with pyridine (4 ml.) and acetic anhydride (4 ml.). After being poured into water, the *product* (0·9 g.) was crystallised from aqueous ethanol, forming needles, m. p. 138—139°, or from ethanol forming plates, m. p. 158°, $[\alpha]_D^{17}$ +17·4° (*c* 1·3 in $CHCl_3$) (Found: C, 51·15; H, 4·9; S, 9·8. $C_{28}H_{32}O_{14}S_2$ requires C, 51·2; H, 4·9; S, 9·7%).

(1R)-1 : 2-5 : 6-*Di*-O-iso*propylidene*-3 : 4-*di*-O-p-*nitrobenzenesulphonylinositol* (Ib).—A solution of (1*R*)-di-*O*-*iso*propylideneinositol[16] (1·0 g.) and *p*-nitrobenzenesulphonyl chloride (3·4 g.) in anhydrous pyridine (10 ml.) was set aside at room temperature for 3 days, then diluted with water. The gum was separated, washed with water, and crystallised from ethanol. Recrystallisation from that solvent gave the *sulphonyl derivative* as plates (2·2 g., 90%), m. p. 171—172°, $[\alpha]_D^{17}$ −62° (*c* 1·0 in $CHCl_3$) (Found: C, 45·55; H, 4·05. $C_{24}H_{24}O_{14}N_2S_2$ requires C, 45·7; H, 4·15%).

The *iso*propylidene groups were removed from the compound (0·71 g.) by 80% aqueous acetic acid (25 ml.) at 100° in 3 hr. Evaporation gave crystals of (1*R*)-3 : 4-di-*O*-*p*-nitrobenzenesulphonylinositol which decomposed above 170°.

(1R)-1 : 2-5 : 6-*Di*-O-iso*propylidene*-3 : 4-*di*-O-*methanesulphonylinositol* (Ic).—(1*R*)-Di-*O*-*iso*propylideneinositol (1·0 g.) and methanesulphonyl chloride (1·76 g.) in anhydrous pyridine (10 ml.) were set aside at room temperature for 16 hr. Water was then added and the precipitate (1·50 g.) recrystallised from ethyl acetate, to give plates of the *dimethanesulphonyl derivative* (1·38 g., 87%), m. p. 260°, $[\alpha]_D^{17}$ −120° (*c* 1·0 in $CHCl_3$) (Found: C, 40·35; H, 5·8. $C_{14}H_{24}O_{10}S_2$ requires C, 40·25; H, 5·7%).

(+)-cyclo*Hex*-5-*ene*-1 : 2/3 : 4-*tetrol* (II).—(1*R*)-1 : 2-5 : 6-Di-*O*-*iso*propylidene-3 : 4-di-*O*-tosylinositol[6] (10 g.) and anhydrous sodium iodide (15 g.) in anhydrous acetone (100 ml.) were heated at 100° for 23 hr. The precipitated sodium toluene-*p*-sulphonate (6·78 g., 99·5%) was separated and washed with acetone. The filtrate was added to light petroleum (b. p. 40—60°) (500 ml.), and the precipitate of iodine and sodium iodide was filtered off. The filtrate was evaporated to a syrup which did not crystallise and was hydrolysed by 50% aqueous acetic acid (40 ml.) for 3 hr. at 100°. The solution was then evaporated to dryness and the residue extracted with cold water (2 × 10 ml.); evaporation of the extracts gave the crude *tetrol* (1·57 g.). After recrystallisation from methanol it was obtained as plates (0·81 g., 32%), m. p. 193°, $[\alpha]_D^{28}$ +332° (*c* 1·9 in H_2O) (Found: C, 49·15; H, 6·8. $C_6H_{10}O_4$ requires C, 49·3; H, 6·9%).

With pyridine and acetic anhydride it gave a gum from which the tetrol was recovered by hydrolysis.

1 : 2-3 : 4-*Di*-O-iso*propylidene*cyclo*hex*-5-*ene*-1 : 2/3 : 4-*tetrol*.—(1*R*)-Di-*O*-*iso*propylidenedi-*p*-nitrobenzenesulphonylinositol (0·63 g.) and anhydrous sodium iodide (1·50 g.) in anhydrous acetone (10 ml.) were heated in a sealed tube at 100° for 13 hr. The precipitated sodium *p*-nitrobenzenesulphonate (0·42 g., 93%) was separated; the filtrate was poured into chloroform, and the chloroform solution washed with sodium thiosulphate solution, dried (Na_2SO_4), and evaporated to dryness. The oily residue was extracted with light petroleum and the extract evaporated to dryness. The residue (0·19 g.) was sublimed twice at *ca.* 60°/1·5 mm., to give

[14] Posternak and Reymond, *Helv. Chim. Acta*, 1955, **38**, 195.
[15] Barker and Bourne, *Adv. Carbohydrate Chem.*, 1952, **7**, 170.
[16] Angyal and Macdonald, *J.*, 1952, 686.

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plates (0·12 g., 52%) of the *compound*, m. p. 60—61° (Found: C, 63·65; H, 7·95. $C_{12}H_{18}O_4$ requires C, 63·7; H, 8·0%).

This product (90 mg.) was hydrolysed by 20% aqueous acetic acid (10 ml.) at 100° in 2 hr. Evaporation gave *cyclo*hex-5-ene-1 : 2/3 : 4-tetrol (60 mg.), m. p. 190°.

Hydroxylation of (+)-cyclo*Hex-5-ene*-1 : 2/3 : 4-*tetrol*.—The unsaturated tetrol (147 mg.) and silver chlorate (64 mg.) were dissolved in water (9 ml.) and 1% osmium tetroxide solution (1 ml.) was added. After being kept for 3 days in the dark, the solution was filtered from the precipitated silver chloride and evaporated to dryness. The residue was sublimed at 0·1 mm., to give *allo*inositol (65 mg., 36%), m. p. 310—320° (decomp.). Dangschat and Fischer [11] record m. p. 270—275°.

The inositol (35 mg.) was heated with acetic anhydride (1 ml.) and pyridine (1 ml.) for 3 hr. at 100°. The mixture was evaporated *in vacuo* and the residue recrystallised from aqueous ethanol, to give *allo*inositol hexa-acetate (75 mg.) as needles, m. p. 143—144° (Found: C, 50·05; H, 5·7. Calc. for $C_{18}H_{24}O_{12}$: C, 50·0; H, 5·6%). The m. p. of authentic *allo*inositol hexa-acetate [7] was not depressed.

(+)-cyclo*Hexane*-1 : 2/3 : 4-*tetrol* (VI).—(+)-*cyclo*Hex-5-ene-1 : 2/3 : 4-tetrol (0·215 g.) in water (10 ml.) was hydrogenated in the presence of 10% palladium–carbon (0·1 g.); after the uptake of 1 mol. of hydrogen, the solution was filtered and evaporated, and the residue (0·20 g.) crystallised from methanol, to give the *tetrol* (0·135 g.) as prisms, m. p. 215°, $[\alpha]_D^{26}$ +72° (*c* 1·14 in H_2O) (Found: C, 48·9; H, 8·2. $C_6H_{12}O_4$ requires C, 48·65; H, 8·15%). For the enantiomorph Posternak and Friedli [10] give m. p. 218°, $[\alpha]_D^{23}$ −73·7° (*c* 11·4 in H_2O).

(±)-1 : 2-3 : 4-*Di*-O-iso*propylidene*epi*inositol*.—The following method is shorter than the previous procedure.[16] *epi*Inositol (10 g.) and anhydrous zinc chloride (50 g.) in acetone (300 ml.) were heated under reflux for 40 hr. After the mixture had cooled, a solution of potassium carbonate (60 g.) in water (50 ml.) was added with good stirring. The precipitated salts were filtered off and washed with acetone (2 × 50 ml.); the filtrate was dried (K_2CO_3) and evaporated. The residual oil was diluted with light petroleum, and the crude crystalline product (4·5 g.) was recrystallised from ethyl acetate, to give the di-*O*-*iso*propylidene derivative (3·66 g., 25%), m. p. 180—181°. By acid hydrolysis of the mother-liquors, about 30% of the *epi*inositol was recovered; acetylation of the mixed zinc and potassium salts with acetic anhydride and zinc chloride gave another 30% of *epi*inositol as the hexa-acetate.

(±)-1 : 2-3 : 4-*Di*-O-iso*propylidene*-5 : 6-*di*-O-p-*nitrobenzenesulphonyl*epi*inositol* (IVb).—The preceding compound (1·00 g.) and *p*-nitrobenzenesulphonyl chloride (2·13 g., 2·5 mol.) in anhydrous pyridine (10 ml.) were set aside at room temperature for one week. The mixture was then diluted with water, and the crude product, which solidified, recrystallised from ethanol, to give the *disulphonyl derivative* (1·92 g., 80%) as plates, m. p. 145° (Found: C, 45·8; H, 4·3%).

(±)-1 : 2 : 3 : 4-*Tetra*-O-*acetyl*-5 : 6-*di*-O-p-*nitrobenzenesulphonyl*epi*inositol*.—The preceding compound was heated in acetic acid (10 ml.) and water (10 ml.) at 100° for 2 hr. to remove the *iso*propylidene groups. The solution was then evaporated *in vacuo* and the crystalline residue heated with acetic anhydride (10 ml.) and pyridine (10 ml.) at 100° for 1 hr. The cooled solution was poured into water: the precipitate solidified and was collected. Recrystallisation from ethanol gave the *tetra-acetate* (2·0 g., 88%) as cubes, m. p. 190° (Found: C, 43·4; H, 3·6. $C_{26}H_{26}O_{18}N_2S_2$ requires C, 43·45; H, 3·65%).

all-cis-1 : 2-3 : 4-*Di*-O-iso*propylidene*cyclo*hex*-5-*ene*-1 : 2 : 3 : 4-*tetrol*.—Di-*O*-*iso*propylidene-di-*p*-nitrobenzenesulphonyl*epi*inositol (0·63 g.) and anhydrous sodium iodide (3·0 g.) in anhydrous acetone (20 ml.) were heated in a sealed tube at 100° for 20 hr. The precipitated sodium salt (0·31 g., 69%) was separated and chloroform was added to the filtrate. The solution was washed with sodium thiosulphate solution, dried (Na_2SO_4), and evaporated. The residual oil (0·33 g.) was extracted with light petroleum (2 × 20 ml.) which left some starting material (0·16 g.) undissolved. The extracts were evaporated and the crude product (104 mg.) was sublimed at 60°/0·2 mm. to give the *tetrol* (60 mg., 26%), m. p. 67—68° (Found: C, 61·8; H, 7·65. $C_{12}H_{18}O_4$ requires C, 63·7; H, 8·0%).

all-cis-1 : 2 : 3 : 4-*Tetra*-O-*acetyl*cyclo*hex*-5-*ene*-1 : 2 : 3 : 4-*tetrol*.—Tetra-*O*-acetyl-di-*O*-*p*-nitrobenzenesulphonyl*epi*inositol (1·0 g.) and anhydrous sodium iodide (2·0 g.) in acetic anhydride (20 ml.) were heated under reflux for 20 hr., then poured into water and, when the acetic anhydride had been hydrolysed, the solution was extracted with chloroform. The chloroform layer was washed with sodium thiosulphate solution, sodium carbonate solution, and water.

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The solvent was dried (Na_2SO_4) and evaporated, and the residue was sublimed at *ca.* 100°/0·1 mm. The sublimate crystallised from light petroleum to give prisms of the *tetra-acetate* (184 mg., 42%), m. p. 102—104° (Found: C, 53·6; H, 5·75. $C_{14}H_{18}O_8$ requires C, 53·5; H, 5·7%).

Deacetylation of the tetra-acetate with sodium methoxide, or hydrolysis of the di-*O-iso*propylidene derivative with aqueous acetic acid, gave the all-*cis-cyclo*hexenetetrol (V) as an oil which was reconverted by acetylation into the tetra-acetate, m. p. 103°.

On hydrogenation the tetrol or its tetra-acetate each absorbed a mol. of hydrogen but the resulting saturated derivatives did not crystallise.

Hydroxylation of all-cis-cyclo*Hex-5-ene*-1 : 2 : 3 : 4-*tetrol* (V).—The tetrol (80 mg.) and silver chlorate (35 mg.) were dissolved in water (4 ml.) and, after the addition of 1% osmium tetroxide solution (1 ml.), were kept in the dark for 24 hr. A paper chromatogram [17] (4 : 1 acetone–water) showed the presence of *allo*inositol, but not of *cis*inositol.

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[17] Angyal, McHugh, and Gilham, *J.*, 1957, 1432.

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70. *Thiadiazoles. Part VI.** 5-*Amino*-3-*hydroxy*-1 : 2 : 4-*thiadiazole Derivatives.*

By Frederick Kurzer and Sheila A. Taylor.

1-Aryl(or -alkyl)-2-thio-4-*iso*biurets and the 2-thiobiurets obtained therefrom by dealkylation are smoothly dehydrogenated by bromine or hydrogen peroxide, to 3-alkoxy(or -hydroxy)-5-aryl(or alkyl)amino-1 : 2 : 4-thiadiazoles. *N*-Aryl-*N'*-cyanothioureas, on treatment with alkaline hydrogen peroxide, similarly afford good yields of 5-arylamino-3-hydroxy-1 : 2 : 4-thiadiazoles. Some properties of the new thiadiazoles are described.

Compounds incorporating the ·C(:NH)·NH·C(:S)· grouping in their structure, including *N*-arylimidoarylthioamides,[1] amidinothioureas,[2] and thioaroylguanidines [3] are cyclised to substituted 1 : 2 : 4-thiadiazoles by a number of oxidising agents. In conformity with this generalisation, 1-substituted 2-thiobiurets are now shown [4] to be convertible into *O*-substituted 5-aryl(or alkyl)amino-3-hydroxy-1 : 2 : 4-thiadiazoles. Goerdeler and Bechlars [5] recently obtained related 3-aryloxy(or -alkoxy)-5-amino-1 : 2 : 4-thiadiazoles from *N*-halogenated *iso*ureas and thiocyanate ions. This synthesis, and the cyclisation of thiobiurets and cyanothioureas outlined in the present paper, provide independent preparative routes.

Biurets required as starting materials were produced by modification of existing methods.[6] Bruce's synthesis [7] of *O*-methyl-1-phenyl-2-thio*iso*biuret (I; R = Ph, Alk = Me) from phenyl *iso*thiocyanate and the *iso*urea was improved by the use of aqueous acetone as medium, in which the reaction proceeded smoothly, and furnished up to 85% yields of the methyl- or ethyl homologues. Contrary to Bruce's observation, such *iso*biurets did not decompose at their melting points or on storage at 0°. Anhydrous conditions were required for production of the 1-alkyl analogues: to the suspension obtained on addition of sodium to acetone,[8] the *iso*urea hydrochloride and methyl *iso*thiocyanate were added successively; the *O*-alkyl-1-methyl-2-thio*iso*biurets (I; R = Me, Alk = Me or Et) were isolated in good yield as the hydrochlorides. These salts could not be satisfactorily

* Part V, *J.*, 1957, 2999.

[1] Ishikawa, *Sci. Papers Inst. Phys. Chem. Res.* (*Tokyo*), 1928, **7**, 237.
[2] Kurzer, *J.*, (*a*) 1955, 1; (*b*) 1955, 2288; (*c*) 1956, 2345; (*d*) 1956, 4524; (*e*) 1957, 2999.
[3] Goerdeler and Fincke, *Chem. Ber.*, 1956, **89**, 1033.
[4] For a preliminary announcement see *Chem. and Ind.*, 1956, 1482.
[5] Goerdeler and Bechlars, *Chem. Ber.*, 1955, **88**, 843.
[6] Kurzer, *Chem. Rev.*, 1956, **56**, 95.
[7] Bruce, *J. Amer. Chem. Soc.*, 1904, **26**, 449.
[8] Slotta, Tschesche, and Dressler, *Ber.*, 1930, **63**, 208.

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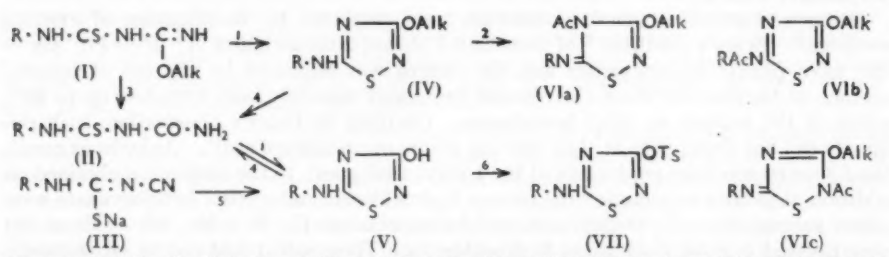
crystallised, since partial dealkylation occurred in boiling solvents under the influence of the mineral acid present. Analytically pure specimens were obtained, however, when the hydrochlorides were slowly reprecipitated from their warm solutions in methanol or chloroform by ether. Purification of the corresponding picrates required similar care. The free base was isolated and purified in the case of the ethyl homologue (I; R = Me; Alk = Et); the low m. p. of the methyl*iso*biuret precluded its isolation in the crystalline state.

It has been stated [7] that hydrogen chloride at 75—90° dealkylates *O*-methyl-1-phenyl-2-thio*iso*biuret to 1-phenyl-2-thiobiuret (II; R = Ph), m. p. 171°. We have been unable to confirm this, but have carried out this reaction in boiling aqueous-ethanolic hydrochloric acid. The m. p. (159—161°) of 1-phenyl-2-thiobiuret thus obtained agrees with that given by Birckenbach and Kraus [9] (161°) for this compound synthesised unequivocally from aniline and carbamoyl *iso*thiocyanate. 1-Methyl-2-thiobiuret was similarly prepared from the *O*-methyl- or *O*-ethyl-*iso*biuret in satisfactory yields.

Oxidation of *O*-alkyl-1-aryl(or alkyl)-2-thio*iso*biurets (I; R = Ph or Me, Alk = Me or Et) gave products which are formulated as 3-alkoxy-5-aryl(or alkyl)amino-1 : 2 : 4-thiadiazoles (IV) on the basis of their mode of formation and their chemical properties (see below). 1-Substituted 2-thiobiurets (II; R = Ph or Me) similarly afforded 5-aryl(or alkyl)amino-3-hydroxy-1 : 2 : 4-thiadiazoles (V). As in the analogous oxidative cyclisation of amidinothioureas,[2] the reaction went to completion almost at once with the calculated quantity of bromine, even at low temperatures. An excess of the oxidising agent had to be avoided, particularly in the aromatic series (I, II; R = Ph), to prevent the formation of non-homogeneous halogenated products. 1-Aryl- and 1-alkyl-substituted thiobiurets (I and II; R = Ph or Me, Alk = H, Me or Et) were cyclised with equal facility: in the latter series, biuret hydrochlorides were employed and were oxidised in aqueous solution.

Alternatively, cyclisations were carried out by means of an excess of hydrogen peroxide, as on previous occasions,[2] in the presence of mineral acid. 1-Phenyl-2-thiobiuret appeared to decompose under these conditions, but was cyclised in alkaline medium. Both methods of oxidation are notable for their speed, the absence of side-reactions, and the high yields of the heterocyclic compounds.

By taking advantage of the well-known conversion of the cyano- into the carbamoyl group under the influence of alkaline hydrogen peroxide,[10] *N*-aryl-*N'*-cyano*iso*thioureas (III; R = Ph or *p*-Me·C_6H_4) in the form of their sodio-derivatives were directly oxidised to 5-arylamino-3-hydroxy-1 : 2 : 4-thiadiazoles (V) in one operation. Although 1-aryl-2-thiobiurets were undoubtedly formed as intermediates, being independently shown to be



Reagents: 1, H_2O or Br_2; 2, Ac_2O or AcCl; 3, HCl; 4, Zn–HCl; 5, H_2O_2–NaOH; 6, *p*-$C_6H_4Me{\cdot}SO_2Cl$–C_5H_5N.

cyclised (to V) under the same conditions, it was not possible to terminate the reaction at this stage (II): the thiadiazole (V; R = Ph) was the only identifiable main product when as little as one molar proportion of hydrogen peroxide was used. Indeed, yields (of V) were not improved by the use of more oxidising agent.

[9] Birckenbach and Kraus, *Ber.*, 1938, **71**, 1492.
[10] Noller, *Org. Synth.*, Coll. Vol. II, p. 586.

The chemical properties of the new thiadiazoles agree with their assigned structures. 5-Anilino-3-hydroxy-1 : 2 : 4-thiadiazole dissolved in dilute alkalis with formation of a sodio-derivative; it was reprecipitated by dilute acids, but was appreciably soluble in more concentrated mineral acids (*e.g.*, 3N-hydrochloric acid), owing to the basic character of the heterocyclic nucleus. The products are phenolic rather than ketonic as they do not give carbonyl derivatives but give purple colours with neutral ferric chloride solution. As with all substituted 3 : 5-diamino-1 : 2 : 4-thiadiazoles so far examined,[2a,b,c,e] reduction by zinc and hydrochloric acid opened the nucleus at the S–N link, reconverting 5-anilino-3-hydroxy-1 : 2 : 4-thiadiazole into 1-phenyl-2-thiobiuret in good yield. The 3-alkoxy-compounds of this series did not give colour reactions with ferric chloride and were insoluble in dilute alkalis and acids. 5-Anilino-3-methoxy-1 : 2 : 4-thiadiazole (but not the 3-ethoxy-homologue) was unexpectedly soluble in hot 3N-sodium hydroxide, from which it was deposited almost quantitatively on cooling; in this respect it resembled 3-amino-5-anilino-1 : 2 : 4-thiadiazole.[2c] Unlike their parent thiobiurets, which were quickly desulphurised by alkaline sodium plumbite, 3-hydroxythiadiazole derivatives resisted the action of this reagent, even in an excess of boiling alkali.

A monoacetyl and a monobenzoyl derivative were obtained from 5-anilino-3-methoxy-1 : 2 : 4-thiadiazole, but no toluene-*p*-sulphonyl derivative could be prepared. Since the site of substitution of acyl groups is most conveniently determined by the reductive hydrolysis of the sulphonyl derivative,[2b,e] the structures of the monoacyl derivatives remain doubtful, formulæ (VIa—c) being possible. 5-Anilino-3-hydroxy-1 : 2 : 4-thiadiazole similarly afforded a diacetyl and dibenzoyl derivative, neither of which gave a colour reaction with ferric chloride: one of the acyl groups has attacked the reactive hydroxyl group, the other occupying one of the possible positions suggested by structures (VIa—c). A monosulphonyl derivative obtained from (V; R = Ph) and an equivalent of toluene-*p*-sulphonyl chloride in pyridine is, for the same reason, formulated as the 3-acyloxy-compound (VII; R = Ph). Goerdeler and Bechlars's 5-amino-3-aralkoxy-1 : 2 : 4-thiadiazoles [5] also yielded monoacetyl derivatives under the same conditions and were designated 5-acetamido-compounds.

Experimental

Light petroleum had b. p. 60—80°.

In the preparation of picrates, aqueous picric acid saturated at 30° (containing 0·06 mole of the reactant per l.) was employed,[11] unless otherwise stated.

O-Ethyl-1-methyl-2-thio*iso*biuret, and 3-methoxy(or ethoxy)-5-methylamino-1 : 2 : 4-thiadiazole, crystallised from benzene, gave high carbon values. One further crystallisation of such specimens from ethanol, though not changing the m. p., gave products of satisfactory composition. Benzene appears to be occluded in crystals of these compounds, but does not form solvates.

All the thiobiurets rapidly gave a precipitate of lead sulphide when heated with sodium plumbite (3N-sodium hydroxide containing a few drops of 10% aqueous lead acetate), but 3-hydroxy-1 : 2 : 4-thiadiazole derivatives resisted this reagent during 2 minutes' boiling.

O-*Methyl*-1-*phenyl*-2-*thio*isobiuret.—To a solution of potassium hydroxide (85%) (13·2 g., 0·2 mole) in water (50 ml.) were added successively *O*-methyl*iso*urea hydrochloride [12] (22·1 g., 0·2 mole) and acetone (100 ml.). The resulting suspension was treated with phenyl *iso*thiocyanate (20·25 g., 0·15 mole), and the rapidly stirred liquid refluxed during 30 min. The acetone was then quickly distilled off under reduced pressure, and the residual two-phase system stirred into ice (300 g.). The collected pale-yellow granular solid was once crystallised from benzene–light petroleum (150 and 20 ml.), and then from benzene. The product formed prisms, m. p. 129—131° (22·2—26·6 g., 71—85%).

O-*Ethyl* 1-*phenyl*-2-*thio*isobiuret.—Condensation of phenyl *iso*thiocyanate (0·15 mole) and *O*-ethyl*iso*urea hydrochloride (0·225 mole) by the above procedure gave a crystalline *product*,

[11] Dolinski, *Ber.*, 1905, **38**, 1836.
[12] Kurzer and Lawson, *Org. Synth.*, 1954, **34**, 67.

which afforded, after crystallisation from benzene, prisms (23·4—26·7 g.), m. p. 98—99° (Found: C, 53·7; H, 6·1; N, 18·7; S, 14·8. $C_{10}H_{13}ON_3S$ requires C, 53·8; H, 5·8; N, 18·8; S, 14·35%).

1-*Phenyl-2-thiobiuret.*—A solution of *O*-methyl-1-phenyl-2-thio*iso*biuret (15·7 g.) in hot ethanol (150 ml.) was treated with concentrated hydrochloric acid (30 ml.) and refluxed until the evolution of methyl chloride was complete (8—12 min.). The solution was stirred into water (1·2 l.), and the separated product collected after storage at 0° for 24 hr. Crystallisation from ethanol–light petroleum (6 and 3 ml. per g.) gave prismatic needles (5·85—6·6 g.) of 1-phenyl-2-thiobiuret, m. p. 159—161° (Found: C, 49·7; H, 4·8. Calc. for $C_8H_9ON_3S$: C, 49·2; H, 4·6%). Partial evaporation of the mother-liquors gave low-melting fractions, from which further small quantities (5—10%) of 1-phenyl-2-thiobiuret were isolated by continued crystallisation.

Use of 2N-ethanolic hydrogen chloride under identical conditions gave similar yields (50—60%), but gave rise to a nauseating and most persistent odour. Hydrolysis of *O*-ethyl-1-phenyl-2-thio*iso*biuret similarly afforded 1-phenyl-2-thiobiuret, m. p. and mixed m. p. 158—160°, albeit in lower yields (28%) (Found: C, 49·5; H, 4·6%).

1-*Phenyl-2-thiobiuret picrate* was slowly deposited (65%) when hot saturated ethanolic solutions of equimolecular quantities of the thiobiuret and picric acid were mixed. It formed yellow leaflets, m. p. 129—131° (from ethanol) (Found: C, 39·0; H, 2·6. $C_8H_9ON_3S,C_6H_3O_7N_3$ requires C, 39·6; H, 2·8%).

5-*Anilino*-3-*methoxy*-1 : 2 : 4-*thiadiazole.*—(*a*) A solution of *O*-methyl-1-phenyl-2-thio*iso*biuret (6·30 g., 0·03 mole) in hot ethanol (75 ml.) was allowed to cool to 35—40°, and rapidly treated, with cooling, with ice-cold freshly prepared M-ethanolic bromine (30 ml.). The solution was decolorised instantly, and crystals separated towards the end of the oxidation. Addition of the mixture to ice-water (750 ml.) converted the suspended solid into a granular precipitate, which was collected, washed with water (m. p. 156—158°; 4·65—5·30 g., 75—85%), and crystallised from acetone–ethanol (10 and 3 ml. per g.) as prismatic needles of 5-*anilino*-3-*methoxy*-1 : 2 : 4-*thiadiazole*, m. p. 158—159° [Found: C, 52·35; H, 4·1; N, 20·2; S, 15·2%; *M* (cryoscopically in thymol), 195. $C_9H_9ON_3S$ requires C, 52·2; H, 4·35; N, 20·3; S, 15·5%; *M*, 207]. The product, though very sparingly soluble in boiling water (approx. 1 g. per l.), was appreciably soluble in hot 3N-aqueous sodium hydroxide and was deposited therefrom unchanged almost quantitatively on cooling.

(*b*) A boiling solution of *O*-methyl-1-phenyl-2-thio*iso*biuret (2·10 g., 0·01 mole) in ethanol (25 ml.) was treated with a mixture of concentrated hydrochloric acid (1 ml., 0·01 mole) and 6% hydrogen peroxide (5·7 ml., 0·01 mole), followed, at three-minute intervals, by two further equivalents of the oxidant. The pink turbid liquid was stirred into ice-water (150 ml.), and the precipitated solid collected after 12 hours' storage at 0°, and crystallised as above, affording 5-anilino-3-methoxy-1 : 2 : 4-thiadiazole (1·5 g., 72%), m. p. and mixed m. p. 158—160° (Found: C, 52·6; H, 4·3; N, 20·6; S, 15·8%). In the absence of mineral acid, the same product was obtained in improved yields (85—90%).

A solution of this thiadiazole (1·03 g., 0·005 mole) in acetic anhydride (10 ml.) was refluxed during 0·5 hr., then stirred into ice-water. The white precipitate, crystallised from acetone–ethanol, consisted of platelets (1·0 g., 80%) of the *monoacetyl derivative*, m. p. 209—210° (Found: C, 52·6; H, 4·4; N, 16·3. $C_{11}H_{11}O_2N_3S$ requires C, 53·0; H, 4·4; N, 16·9%). Interaction of the thiadiazole (0·005 mole) with benzoyl chloride (1·40 g., 0·01 mole) in pyridine (10 ml.) at 100° during 20 min., followed by addition to ice–hydrochloric acid, gave a crude product which was extracted with hot water (removal of benzoic acid) and crystallised from acetone–ethanol. The resulting *monobenzoyl derivative* formed needles, m. p. 180—181° (1·27 g., 82%) (Found: C, 61·4; H, 4·2; S, 9·7. $C_{16}H_{13}O_2N_3S$ requires C, 61·7; H, 4·2; S, 10·3%).

The reactant, after treatment with toluene-*p*-sulphonyl chloride (1 or 2 mols.) in pyridine at 95—100° during 5 min., was mostly recovered unchanged. The use of 2 or 4 mols. of sulphonyl chloride during 1 hr. gave intractable oils or granular products, while intermediate conditions gave mixtures of starting material and uncrystallisable oils. Hinsberg and Kessler's [13] procedure also failed to yield a sulphonyl derivative.

5-*Anilino*-3-*ethoxy*-1 : 2 : 4-*thiadiazole*, obtained (*a*) in 75—80% yield by cyclising *O*-ethyl-1-phenyl-2-thio*iso*biuret with bromine, crystallised from ethanol (20 ml. per g.) as needles, m. p. 167—168° [Found: C, 53·9; H, 5·05; N, 18·5; S, 14·2%; *M* (cryoscopically in thymol), 230. $C_{10}H_{11}ON_3S$ requires C, 54·3; H, 5·0; N, 19·0; S, 14·5%; *M*, 221] or (*b*) by oxidation of

[13] Hinsberg and Kessler, *Ber.*, 1905, **38**, 906.

the *O*-ethyl*iso*biuret by hydrogen peroxide in the presence of mineral acid, similarly afforded 80% yields of the same 1 : 2 : 4-thiadiazole, m. p. and mixed m. p. 166—168° (Found: C, 54·8; H, 4·9%). Neither this compound nor the 3-methoxy-analogue (IV; R = Ph, Alk = Me) gave a colour with neutral ferric chloride solution.

5-Anilino-3-hydroxy-1 : 2 : 4-thiadiazole.—From 1-phenyl-2-thiobiuret. (*a*) A stirred solution of 1-phenyl-2-thiobiuret (5·85 g., 0·03 mole) in ethanol (45 ml.) at 35—40° was treated (with external cooling) during 1 min., with 1M-bromine in chloroform (30 ml.), which was decolorised instantly. The liquid was added to water (300 ml.), and the aqueous phase (containing a little suspended solid) decanted from the separated chloroform layer, from which the solvent was then evaporated rapidly at room temperature. The residual white product was recombined with the aqueous suspension, and the solid collected. It crystallised from acetone–ethanol, and then ethanol alone (100 ml. per g.), giving prisms of *5-anilino-3-hydroxy-1 : 2 : 4-thiadiazole*, m. p. 210—212° (decomp., somewhat subject to the rate of heating) (yield, including material from the mother-liquors, 3·5—4·35 g., 60—75%) [Found: C, 50·0 49·8; H, 3·5, 3·7; N, 21·9, 21·6; S, 16·7, 16·4%; *M* (cryoscopically in thymol), 200, 180. $C_8H_7ON_3S$ requires C, 49·7; H, 3·6; N, 21·8; S, 16·6%; *M*, 193].

The thiadiazole was sparingly soluble in boiling water, and crystallised in needles therefrom. It dissolved freely in warm N-sodium hydroxide and was reprecipitated by the addition of dilute acid, but was also soluble in more concentrated (*e.g.*, 3N-hydrochloric) acid. Warm solutions of the thiadiazole (0·001 mole) in 3N-sodium hydroxide (5 ml.) deposited, on cooling, almost quantitatively the sodium derivative, as prisms (from a little boiling water), m. p. 208—210° (decomp.).

The product did not yield a 2 : 4-dinitrophenylhydrazone on treatment with Brady's reagent, or an oxime on treatment with hydroxylamine, under the usual conditions. It gave a violet-purple colour with ferric chloride in methanolic, but not in aqueous, solution.

(*b*) A solution of 1-phenyl-2-thiobiuret (1·95 g., 0·01 mole) in water (20 ml.) containing sodium hydroxide (0·80 g., 0·02 mole) was treated with 6% hydrogen peroxide (8·5 ml., 0·015 mole). The liquid, the temperature of which rose spontaneously, was kept at 50° during 5 min., then cooled, and the separated solid collected at 0° (filtrate A). Its solution in hot water (75 ml.) was acidified with dilute acetic or hydrochloric acid, and the precipitated solid (m. p. 207—208°; 1·45 g., 75%) crystallised as above, the thiadiazole, m. p. and mixed m. p. 210—212°, being obtained (Found: C, 50·2; H, 3·3%). Filtrate A gave a further 5—10% of the same product on acidification.

From N-cyano-N′-phenylthiourea. (i) Sodium *N*-cyano-*N*′-phenyl*iso*thiourea [14] (1·99 g., 0·01 mole), nearly dissolved in a mixture of ethanol (5 ml.) and aqueous sodium hydroxide (3N; 3·3 ml., 0·01 mole), was treated, with stirring, between 45 and 50°, dropwise with 6% hydrogen peroxide (20 ml., 0·035 mole). The resulting suspension was kept at 50° during another 15 min., then diluted with ethanol (5 ml.) and cooled, and the sodium salt was collected at 0° (filtrate A). Treatment as described under (*b*) afforded the thiadiazole (m. p. and mixed m. p. 210—212°; 0·81 g., 42%). Filtrate A did not afford more product on acidification, with or without previous partial evaporation in a vacuum.

In the absence of ethanol, or of the extra equivalent of alkali, or at 30—35°, the yield fell to 20—30%. Above 50°, the temperature was difficult to control and complete decomposition occurred, with formation of intractable gums. The intermediate 1-phenyl-2-thiobiuret could not be isolated by the use of only 1 equivalent of the oxidising agent: the thiadiazole was again obtained (in 38% yield).

(ii) A solution of cyanamide (4·2 g., 0·1 mole) in water (6 ml.) was successively treated with 10N-sodium hydroxide (10 ml., 0·1 mole) and phenyl *iso*thiocyanate (6·75 g., 0·05 mole). Ethanol (10 ml.) was added, until the system consisted of a single phase, which was next heated on the steam-bath during 18 min. The resulting yellow liquid, diluted with water (40 ml.) and cooled, was treated at 30—40° with 6% hydrogen peroxide (0·075 mole) during 5—10 min., and kept at 45° during 15 min. The separated sodium salt, collected at 0°, was converted into 5-anilino-3-hydroxy-1 : 2 : 4-thiadiazole (5·40 g., 56%), m. p. and mixed m. p. 210—212° (decomp.), as described above. The identity of this 1 : 2 : 4-thiadiazole with specimens obtained by methods (*a*) and (*b*) was confirmed by a comparison of their dibenzoyl derivative, m. p. and mixed m. p. 180—184°.

Derivatives. 5-Anilino-3-hydroxy-1 : 2 : 4-thiadiazole (0·965 g., 0·005 mole), heated in pyridine (10 ml.) with toluene-*p*-sulphonyl chloride (1·14 g., 0·006 mole) at 100° during 20 min.

[14] Fromm and Wenzl, *Ber.*, 1922, **55**, 805.

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and stirred into ice–hydrochloric acid, gave a flocculent precipitate. After three crystallisations from benzene, it consisted of prisms of *5-anilino-3-toluene-*p*-sulphonyloxy-*1 : 2 : 4*-thiadiazole*, m. p. 160—162° (0·52 g., 30%) (Found: C, 51·6; H, 3·3; N, 12·1; S, 17·9. $C_{15}H_{12}O_3N_3S_2$ requires C, 51·9; H, 3·75; N, 12·1; S, 18·4%). The thiadiazole gave (on treatment as described for the 5-methoxy-analogue, see above) needles (from acetone–ethanol) of a *diacetyl derivative*, m. p. 253—255° (somewhat subject to the rate of heating) (72%) (Found: C, 51·9; H, 3·4; N, 15·5; S, 11·7. $C_{12}H_{11}O_3N_3S$ requires C, 52·0; H, 4·0; N, 15·2; S, 11·55%). Analogously, there was prepared the *dibenzoyl derivative*, forming prisms (from benzene), m. p. 182—184° (somewhat subject to the rate of heating) (50%) (Found: C, 66·1; H, 3·4; N, 10·55; S, 7·95. $C_{22}H_{15}O_3N_3S$ requires C, 65·8; H, 3·7; N, 10·5; S, 8·0%). None of the derivatives gave a colour reaction with neutral ferric chloride solution.

Reduction. (*a*) A refluxing suspension of 5-anilino-3-hydroxy-1 : 2 : 4-thiadiazole (3·86 g., 0·02 mole) and zinc turnings (6 g.) in ethanol (60 ml.) was treated dropwise with concentrated hydrochloric acid (5 ml.) during 8 min., and refluxing continued for another 4 min. The solution was decanted, the residual zinc extracted with more boiling ethanol (4 × 5 ml.), and the whole liquid reduced to a third of its bulk in a vacuum, then stirred into ice–water (100 ml.). The collected solid (filtrate F), on crystallisation from ethanol, consisted of 1-phenyl-2-thiobiuret (2·65 g., 68%), m. p. and mixed m. p. 157—159°. Filtrate F did not contain aniline. (*b*) 5-Anilino-3-methoxy-1 : 2 : 4-thiadiazole (0·02 mole), when similarly reduced, during 6 min., gave a crude product (2·5 g.), which yielded, on fractional crystallisation from ethanol and benzene–acetone, small quantities of 1-phenyl-2-thiobiuret (0·90 g., 23%), m. p. and mixed m. p. 158—159°. The aqueous filtrates (corresponding to F, as immediately above) contained aniline, which was isolated from the basified solution by ether-extraction and identified as the benzoyl derivative (15%).

*3-Hydroxy-5-*p*-tolylamino-*1 : 2 : 4*-thiadiazole*.—An experiment with *p*-tolyl *iso*thiocyanate (7·45 g., 0·05 mole) according to procedure (ii, above) gave the sodium salt, which was collected at 0°. Dissolution in hot water (150 ml.) (addition of a little alkali), filtration, and acidification with concentrated hydrochloric acid (to Congo-red; ice-cooling) gave a precipitate (m. p. 203—208°; 4·95 g., 48%). This afforded, from 1 : 1 acetone–ethanol, prisms of *3-hydroxy-5-*p*-tolylamino-*1 : 2 : 4*-thiadiazole*, m. p. 212—214° (decomp., somewhat subject to the rate of heating) (Found: C, 52·5; H, 4·1; N, 20·0; S, 15·2. $C_9H_9ON_3S$ requires C, 52·2; H, 4·35; N, 20·3; S, 15·5%).

*1 : O-Dimethyl-2-thio*isobiuret.—Sodium (3·22 g., 0·14 g.-atom) was added to cooled anhydrous acetone (125 ml.) during 8—12 min. The resulting orange-red suspension was treated, at 35—40°, with powdered methyl*iso*urea hydrochloride (14·4 g., 0·13 mole) followed by methyl *iso*thiocyanate (8·0 g., 0·11 mole, dissolved in 10 ml. of acetone). The stirred suspension was heated to boiling during 5 min., and refluxed until smelling no longer of *iso*thiocyanate (30—45 min.). The bulk of the acetone was removed under reduced pressure, the residual thick suspension diluted with water (75 ml.), and the resulting two-phase system separated. The aqueous layer was extracted with ether (2 × 30 ml.), and the extracts were added to the orange (upper) layer, which was diluted with more ether (100—150 ml.), washed with warm water (3 × 10 ml.), and dried (Na_2SO_4; 24 hr.). To the filtered orange solution, 3·5N-ethanolic hydrochloric acid (28 ml., 0·1 mole) was slowly added, and the precipitate collected after several hours' storage at 0° (on a large Buchner funnel) and washed with ether. The white microcrystalline product, dried in a vacuum, was *1 : O-dimethyl-2-thio*isobiuret hydrochloride, m. p. 154—156° (after sintering at 145—150°) (13·1—14·5 g., 65—72%). Reprecipitation of the product by ether from its warm methanolic solution did not improve the m. p., but gave a nearly pure specimen (Found: C, 26·9; H, 5·4; Cl, 19·0. $C_4H_9ON_3S,HCl$ requires C, 26·2; H, 5·45; Cl, 19·3%). The hydrochloride was soluble in boiling methanol and ethanol but, owing to partial dealkylation, did not crystallise satisfactorily therefrom. The product gave a black precipitate with sodium plumbite.

The base, liberated by caustic alkali, was low-melting and was not obtained crystalline.

Treatment of the hydrochloride (0·37 g., 0·002 mole) in water (3 ml.) with picric acid (0·002 mole) precipitated the *picrate* (85%) which consisted, after *rapid* crystallisation from ethanol (15 ml. per g., containing a few drops of water), of yellow needles, m. p. 154—156° (decomp., after sintering at 136°) (Found: C, 32·3; H, 3·1; N, 22·6; S, 8·2. $C_4H_9ON_3S,C_6H_3O_7N_3$ requires C, 31·9; H, 3·2; N, 22·3; S, 8·5%).

*O-Ethyl-1-methyl-2-thio*isobiuret.—Interaction of sodium, ethyl*iso*urea hydrochloride, and

methyl *iso*thiocyanate (as described for the methyl *iso*-homologue, except for the time of refluxing, which was 15 min.) afforded, by the same technique, the crude hydrochloride, m. p. 99—101° (decomp.) (60—70%). Crystallisation, by dissolution in warm chloroform (10 ml. per g.) and dilution with a little ether, gave white *O-ethyl-1-methyl-2-thioisobiuret hydrochloride*, m. p. 105—106° (decomp.) (Found: C, 30·3; H, 6·3; N, 21·5; Cl, 17·9. $C_5H_{11}ON_3S,HCl$ requires C, 30·4; H, 6·1; N, 21·3; Cl, 18·0%).

The hydrochloride was converted almost quantitatively into the *picrate*, which formed yellow prisms, m. p. 125—126° (decomp.) (from ethanol) (Found: C, 33·4; H, 3·4. $C_5H_{11}ON_3S,C_6H_3O_7N_3$ requires C, 33·8; H, 3·6%).

The crude hydrochloride obtained in an experiment starting with 0·11 mole of methyl *iso*thiocyanate was treated in water (30 ml.) with 3N-sodium hydroxide (20 ml.). The precipitated oil solidified presently, was collected, washed with a little water, air-dried, and crystallised successively from benzene (5 ml. per g.) and aqueous ethanol. The resulting *O-ethyl-1-methyl-2-thioisobiuret* formed large prisms (from benzene) or platelets (from aqueous ethanol), m. p. 90—91° (yield, including material from filtrates, 62%) (Found: C, 37·6; H, 6·8; S, 20·2. $C_5H_{11}ON_3S$ requires C, 37·3; H, 6·8; S, 19·9%).

1-Methyl-2-thiobiuret.—1 : *O*-Dimethyl-2-thio*iso*biuret hydrochloride (5·5 g.) rapidly dissolved in methanol (60 ml.) and concentrated hydrochloric acid (12 ml.) on boiling, which was continued until evolution of methyl chloride ceased (12—15 min.). The liquid was evaporated in a vacuum at the lowest possible temperature, in two stages to small bulk (approx. 20 and 5 ml., respectively), and the separated crude product each time collected at 0° (total, 3—3·5 g.). One crystallisation from boiling water (4—6 ml. per g.) gave a white crystalline powder of *1-methyl-2-thiobiuret*, m. p. 172—174° (decomp., after sintering slightly about 160°) (1·8—2·1 g., 45—52%), which consisted, after two further crystallisations from water, of needles, m. p. 174—175° (decomp.) (Found: C, 26·9; H, 5·25; N, 31·1. $C_3H_7ON_3S$ requires C, 27·1; H, 5·3; N, 31·6%). 1-Methyl-2-thiobiuret is highly soluble in methanol and ethanol, and sparingly so in benzene and light petroleum. It gives a white precipitate with silver nitrate in the presence of nitric acid, and an immediate black precipitate of lead sulphide with sodium plumbite and excess of alkali. It crystallises unchanged from boiling 3N-hydrochloric acid.

Hydrolysis of *O*-ethyl-1-methyl-2-thio*iso*biuret (in ethanol, duration 18—20 min.) similarly gave 1-methyl-2-thiobiuret, m. p. 172—174° (decomp., after sintering about 165°), in improved yield (68%).

3-Methoxy-5-methylamino-1 : 2 : 4-thiadiazole.—A solution of 1 : *O*-dimethyl-2-thio*iso*biuret hydrochloride (crude, 3·67 g., 0·02 mole) in warm water (10 ml.) was treated with M-bromine (in chloroform, 20 ml.). The colourless two-phase system was separated, and the aqueous layer made alkaline with 3N-sodium hydroxide. The separated solid was collected at 0° (m. p. 118—121°; 1·6—1·8 g., 55—62%) and crystallised successively from benzene (5 ml. per g.) and methanol, affording needles of *3-methoxy-5-methylamino-1 : 2 : 4-thiadiazole*, m. p. 120—121° (Found: C, 33·55; H, 4·9; N, 29·2, 28·7; S, 22·1. $C_4H_7ON_3S$ requires C, 33·1; H, 4·8; N, 29·0; S, 22·1%). Evaporation of the chloroform layer, followed by reprecipitation of the residue from its solution in dilute hydrochloric acid by alkali gave another 3—6% of the crude thiadiazole.

Addition of picric acid (0·0025 mole) to the thiadiazole (0·36 g., 0·0025 mole) in warm water (15 ml.) gave a precipitate (0·66 g., 71%), which consisted, after crystallisation from aqueous ethanol (75%), of yellow prisms of the *picrate*, m. p. 155—157° (Found: C, 32·2; H, 2·7; N, 22·4; S, 8·1. $C_4H_7ON_3S,C_6H_3O_7N_3$ requires C, 32·1; H, 2·7; N, 22·5; S, 8·6%).

3-Ethoxy-5-methylamino-1 : 2 : 4-thiadiazole.—Oxidation of *O*-ethyl-1-methyl-2-thio*iso*biuret hydrochloride (as described for the methyl homologue) gave a product (m. p. 121—123°; yield 35 and 45%, from the aqueous and the chloroform phase, respectively) which, after successive crystallisation from benzene and ethanol, consisted of needles of the *thiadiazole*, m. p. 122—123° (Found: C, 37·8; H, 5·65; N, 26·5. $C_5H_9ON_3S$ requires C, 37·7; H, 5·7; N, 26·4%).

3-Hydroxy-5-methylamino-1 : 2 : 4-thiadiazole.—1-Methyl-2-thiobiuret (1·0 g., 0·0075 mole) in methanol (20 ml.) was treated with M-bromine in chloroform (7·5 ml.) below 30°, the white crystalline precipitate collected after 3 hours' storage at 0°, and the filtrate evaporated at room-temperature in a vacuum to recover further small quantities of product. The combined solids were dissolved in 3N-sodium hydroxide (4 ml.) and slowly reprecipitated with 3N-hydrochloric acid (until just acid to litmus). The collected *product* (0·37 g., 38%), when crystallised from ethanol, consisted of off-white opaque granules, m. p. (decomp.) dependent on the rate of

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heating* (Found: C, 27·7; H, 4·0; N, 32·5; S, 24·9. $C_3H_3ON_3S$ requires C, 27·5; H, 3·8; N, 32·1; S, 24·4%). Solutions of the compound in methanol gave a purple colour with ferric chloride solution. The following derivatives were obtained by the usual methods: the *picrate* (85%) formed yellow clusters of needles, m. p. 168—169° (decomp.), from 1 : 1 aqueous ethanol (Found: C, 30·3; H, 2·3. $C_3H_3ON_3S,C_6H_3O_7N_3$ requires C, 30·0; H, 2·2%). The *dibenzoyl derivative* (54%) consisted of needles (from acetone–ethanol), m. p. 203—204° (decomp.; somewhat subject to the rate of heating) (Found: C, 60·1; H, 3·7. $C_{17}H_{13}O_3N_3S$ requires C, 60·2; H, 3·8%).

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* When heated from room temperature, samples of the thiadiazole began sintering at 180° and continued to decompose slowly though incompletely up to 280°; when inserted into the bath at 240°, specimens decomposed instantly; at 220° and 200° they did so after a time lag.

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71. *Equilibrium Constants for the Reaction between Bromine and Bromide Ions at 5°, 25°, and 35° in Aqueous Medium of Constant Ionic Strength and Acidity.*

By D. B. SCAIFE and H. J. V. TYRRELL.

Bromine combines with bromide ions to form principally the tribromide ion Br_3^-, and this reaction can be used to measure free bromide-ion concentrations in other complex equilibria involving bromide ions provided that the formation constants for the bromine–bromide ion system are known with sufficient accuracy. The precise measurement of these constants at an ionic strength of $I = 0{\cdot}5$ and an acid concentration of 0·01 molal at three temperatures is described. This was a necessary preliminary to the study of the mercuric bromide–bromide ion system reported in the succeeding paper.

BROMINE forms donor–acceptor complexes with bromide ions of the forms Br_3^- and Br_5^-, the former being the more important. The concentration of free bromine in a solution containing both bromine and bromide ions can be accurately determined by allowing the bromine to come to equilibrium, through the vapour phase, with a similar solution not containing bromide ions. The equilibrium activity of bromine in this solution is equal to the activity of free bromine in the solution containing bromide ions. If the activity coefficients are known, or are the same in both solutions, the concentration of the free bromine in the complexed solution can be found easily and precisely, by analysing the bromide-free solution. This was the basis of a method used in earlier studies of this equilibrium system.[1,2] If the constants for this system can be found with sufficient accuracy, the concentration of free bromide ions in a solution containing both bromine and bromide ions can be calculated. Thus, the bromine–bromide ion system could, in principle, be used to study other complex equilibria involving bromide ions by adding bromine to the mixture, measuring the total and free bromine concentrations, and using these to calculate the free bromide-ion concentration. This method is more laborious than direct measurement of the free bromide-ion concentration, for example, with an electrode system reversible to bromide ions, but is valuable where such methods cannot be applied. Its development required accurate measurements of the equilibrium constants of the bromine–bromide ion system under the appropriate experimental conditions as now described; an application is described in the following paper.

[1] Warley, *J.*, 1905, **88**, 1107.
[2] Jones and Baeckström, *J. Amer. Chem. Soc.*, 1934, **56**, 1517.

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The main product in the reaction between bromine and bromide ions is the tribromide ion:

$$Br_2 + Br^- \rightleftharpoons Br_3^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

An equilibrium constant χ_3 can be defined for this reaction as

$$\chi_3 = [Br_3^-]/([Br_2][Br^-])$$

However, earlier studies,[1,3,4] culminating in that of Jones and Baeckström,[2] showed that the following reactions cannot always be neglected:

$$2Br_2 + Br^- \rightleftharpoons Br_5^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$$Br_2 + H_2O \rightleftharpoons H^+ + Br^- + HBrO \quad . \quad . \quad . \quad . \quad . \quad (3)$$

For these, equilibrium constants χ_5 and χ_h can be defined as follows:

$$\chi_5 = [Br_5^-]/([Br^-][Br_2]^2)$$

$$\chi_h = [H^+][Br^-][HBrO]/[Br_2]$$

In much earlier work activity coefficients were neglected; later they were included [2,4] by using data on the activity coefficient of bromine in salt solutions in which no complex formation occurred, and assuming the activity coefficients of the singly charged species Br^-, Br_3^- to be equal as a first approximation. In all our experiments, a solvent medium of constant acidity and of high and almost constant ionic strength was used. The slight acidity helps to suppress the hydrolysis reaction (3), and the constant ionic strength to ensure that activity coefficients are independent of changes in concentration of the complex species. Since the main object was to use the equilibrium constants to study the mercuric bromide–bromide ion system, the conditions used were those which had been adopted in the only previous modern study [5] of this system, except that the molal scale of concentration replaced the molar one. All solutions were therefore 0·01 molal in perchloric acid, and a total ionic strength of $I = 0{\cdot}5$ was maintained by addition of sufficient sodium perchlorate. The equilibrium was examined for concentration ranges which were of use in the investigation of the mercuric bromide–bromide ion system, namely 20—300 mmoles of sodium bromide per 1000 g. of solvent and at bromine concentrations which gave equilibrium concentration differences between the bromide-rich and bromide-free solutions which could be measured with reasonable accuracy.

Experimental

A glass equilibrator, very similar to Jones and Kaplan's,[6] was used to measure the equilibrium distribution of bromine between the bromide-rich and bromide-free solutions. The apparatus is so constructed that rotation about an axis inclined at a small angle to the vertical causes the vapour to circulate through each solution in turn while preventing direct contact between them. Each separate solution compartment could be filled and emptied through ground-joints normally closed with a stopper lubricated with Fluorolube W grease. It was necessary to rotate the equilibrator in a constant-temperature bath ($\pm 0{\cdot}1°$ or better) for 48 hr. to ensure that equilibrium had been attained at all temperatures used.

About 100 g. each of the following solutions were prepared for each experiment: (i) x mmoles of sodium bromide, 10 mmoles of perchloric acid per 1000 g. of water, and sufficient sodium perchlorate to give an ionic strength of 0·5 on the molality scale, and (ii) as (i) without sodium bromide.

A total of 12—14 mmoles of liquid bromine were usually added to both solutions in approximately the proportions expected to be present after equilibration. The solutions were

[3] Jakowkin, *Z. phys. Chem.*, 1895, **18**, 585; 1896, **20**, 193; Lewis and Randall, *J. Amer. Chem. Soc.*, 1916, **38**, 2348; Linhart, *ibid.*, 1918, **40**, 158; Jones and Hartmann, *Trans. Amer. Electrochem. Soc.*, 1916, **30**, 295; Bray and Connolly, *J. Amer. Chem. Soc.*, 1911, **33**, 1485; Lewis and Storch, *ibid.*, 1917, **39**, 2544; Sherrill and Izard, *ibid.*, 1928, **50**, 1665.

[4] Griffith, McKeown, and Winn, *Trans. Faraday Soc.*, 1932, **28**, 101.

[5] Bethge, Jonevall-Westöö, and Sillén, *Acta Chem. Scand.*, 1948, **2**, 828.

[6] Jones and Kaplan, *J. Amer. Chem. Soc.*, 1928, **50**, 1600.

then put in the two sides of the equilibrator which was allowed to come to thermal equilibrium in the thermostat before inserting the stoppers. After 48 hours' rotation, the contents were analysed. To obtain consistent results Jones and Baeckström's methods [2] were modified. The contents of both compartments were forced simultaneously into separate receivers with compressed air saturated with bromine vapour to approximately the equilibrium pressure; the first few ml. were discarded, the bulk of the rest passed into collecting flasks, fitted with side-arms of the type designed by Jones and Baeckström, and a little was left in the equilibrator. If samples were removed successively from the equilibrator, a slight progressive loss of bromine occurred. The collecting flask contained about 20 ml. of saturated sodium iodide solution, and the side arm was packed with small glass helices moistened with the same solution and a little solid sodium hydrogen carbonate. As the receiving flasks were filled the air was displaced through the side arm, any trace of bromine vapour in it being trapped by the iodide solution. When the addition of the bromine solution was complete, the acid solution in the flask was neutralised by tilting it so that the contents ran into the side arm and reacted with the solid hydrogen carbonate. Preliminary experiments showed that the excess of iodide was oxidised sufficiently rapidly in acid solution, by dissolved air, to give inaccurate results unless the contents of the flask were neutralised immediately after addition of the bromine solution. Addition of this to an initially alkaline iodide solution also gave anomalous results (cf. ref. 2). The weight of bromine solution added was found by weighing the receiver immediately before adding the bromine solution, and again after neutralisation. The loss of weight due to evolution of carbon dioxide in the neutralisation was negligible (about 10 mg., or 25% of the theoretical amount, in a total solution weight of over 100 g.). Since the weight of the contents of the flask, including those of the side arm, had been found initially, the weight dilution factor of the transferred bromine solution could be determined. After estimating each iodine solution in terms of the concentration per 1000 g. of solution, we found the concentration of bromine in a known weight of the original solution at equilibrium by using this weight dilution factor. Since the weight of the other constituents in the original solution was known these bromine concentrations could easily be converted to the molal scale which was used throughout.

The iodine liberated from the sodium iodide was estimated by weight titration with a standard sodium arsenite solution in presence of a sodium hydrogen carbonate buffer. A sample of the iodine solution was weighed into a flask containing about 2 g. of solid sodium hydrogen carbonate, and a sodium arsenite solution, containing about 0·075 equiv. per 1000 g. of solution, added from a simple weight burette until the solution was pale yellow. The remaining iodine was estimated by adding sodium arsenite solution of about one fifth of the concentration of that used for the bulk of the titration, from a microburette, starch solution being used as indicator. The density of this dilute solution was assumed to be unity, and the volume added equal to the weight. The standard arsenite solution was prepared from " AnalaR " arsenic oxide by Vogel's method,[7] except that the solution was made up to a known total weight. Three estimations were carried out on each iodine solution, the spread being always less than 0·1%.

Sodium bromide, B.D.H. Laboratory Reagent grade, was recrystallised thrice from distilled water, and the resulting hydrated crystals dehydrated over sodium hydroxide in a vacuum desiccator. Sodium perchlorate, B.D.H. Laboratory Reagent grade, contains principally chloride as an impurity which was effectively removed by recrystallisation twice at 80°. The anhydrous salt thus formed was dried (NaOH). " AnalaR " perchloric acid was used without purification; the solutions used in the equilibrator were made up by adding known weights of a diluted stock solution of known molality. Bromine was prepared from " AnalaR " potassium bromide by oxidation with chromic acid and distillation.[8] The initial 1% of distillate contained iodine from any iodide impurities present in the bromide, and was discarded. Sufficient chromic acid for the oxidation of about 95% of the bromide present was added in all; any chloride impurities remained unoxidised and the bulk of the bromine collected was therefore free from both chlorine and iodine.

Theory

In solutions containing bromide ions, particularly when they are slightly acid, the hydrolysis reaction (3) can be neglected. This was not true for the bromide-free solutions.

[7] Vogel, " Quantitative Inorganic Analysis," p. 416, Longmans, Green and Co., London, 1943.
[8] Robinson and Briscoe, *J.*, 1925, **127**, 142.

However there are no data on the appropriate hydrolysis constants for the conditions used here, and the necessary correction was made as follows. Initially only reactions (1) and (2) are considered, with the following notation: $[Br_2^F]$ ≡ concentration of free bromine in the complexing solution (= measured concentration of bromine in the bromide-free solution if hydrolysis is neglected); $[Br_2^T]$ ≡ total concentration of bromine in the complexing solution; $[Br_2^C] = [Br_2^T] - [Br_2^F]$ ≡ concentration of combined bromine, obtained directly from the measured quantities; $[Br_T^-]$ ≡ known total bromide concentration in the complexing solution; $[Br_C^-]$ ≡ combined bromide-ion concentration; and $[Br_F^-]$ ≡ free bromide-ion concentration.

It is obvious that

$$[Br_3^-] = [Br_2^C] - 2[Br_5^-] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

$$[Br_C^-] = [Br_3^-] + [Br_5^-] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

From eqn. (4) and (5) it follows that

$$[Br_C^-] = [Br_2^C] - [Br_5^-] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

Also,

$$[Br_F^-] = [Br_T^-] - [Br_C^-] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

From eqn. (4) and the definition

$$\chi_{3,5} = \chi_5/\chi_3 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

it can be seen that

$$[Br_5^-] = [Br_3^-][Br_2^F] \cdot \chi_{3,5} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

Extension of this argument shows that the following relation must exist:

$$\alpha = -\beta \cdot \chi_{3,5} + 1/\chi_3 \cdot \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

where α and β are defined as the following combinations of experimentally accessible quantities:

$$\alpha \equiv \frac{[Br_2^F]([Br_T^-] - [Br_2^C])}{[Br_2^C]}$$

$$\beta \equiv \frac{[Br_2^F]^2(2[Br_T^-] - [Br_2^C])}{[Br_2^C]}$$

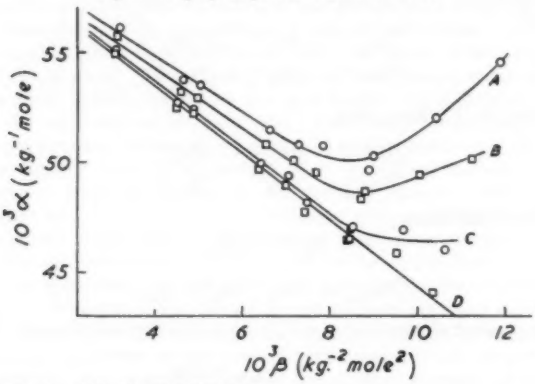
If the ionic strength, and hence the activity coefficients are kept constant throughout, both $\chi_{3,5}$ and χ_3 are true constants, and a plot of α against β should be straight. When the measured concentration of bromine in the bromide-free solution was identified with $[Br_2^F]$ it was found that this was not so. This was because some hydrolysis occurred in the bromide-free solution according to reaction (3), accompanied by complex formation between the liberated bromide ions and the bromine present. However the hydrolysed and complexed bromine, together with the free bromine, were all analysed as bromine in an amount which may be designated as $[Br_2^F]^*$. This was greater than the true free bromine concentration $[Br_2^F]$, and it was the use of $[Br_2^F]^*$ instead of $[Br_2^F]$ which led to the observed deviations from linearity in the plot of α against β. With an approximate value for χ_3 and trial values of χ_h it was possible to apply a correction to $[Br_2^F]^*$, the appropriate value of χ_h selected being that which made α a linear function of β. According to eqn. (10), the slope of this line should be $-\chi_{3,5}$, and the intercept $1/\chi_3$. In practice, it was found preferable to calculate values of χ_3 as follows. Using the value of $\chi_{3,5}$ obtained from the slope, we calculated $[Br_5^-]$ for a given experiment from eqn. (9). Using this, we obtained $[Br_3^-]$ from eqn. (4), and the free bromide concentration from (6) and (7). A value for χ_3 was then calculated. A series of experimental observations led to a set of values of χ_3 from which the mean and the standard deviation of the mean were estimated.

Results

(i) At 25°.—The results for this temperature are displayed in Table 1. Columns 1, 3, and 8 are the experimental quantities. If no correction was made for hydrolysis, the relation between

α and β was not linear (Figure, curve *A*). Using an approximate value of $\chi_3 = 17$ kg. mole^{-1} and the following hydrolysis constants in turn: $5{\cdot}9 \times 10^{-9}$ kg.$^{-2}$ mol.^{2} (experimental, Jones and Baeckström [2]), four times this value, and six times this value, we obtained curves *B*, *C*, and *D* of the Figure. As the hydrolysis correction was increased, the plot of α against β tended towards linearity, and became satisfactorily linear in curve *D*. Although the correction used was some six times that expected from Jones and Baeckström's experimental value for the hydrolysis, it has been employed here to correct $[Br_2^F]^*$ to the $[Br_2^F]$ figures shown in column 2 of Table 1. Only by this means could the principal equilibria be put in the simple form

Influence of hydrolysis corrections at 25°.



Curve *A*. (○) Uncorrected data.
Curve *B*. (□) Corrected, by using $\chi_h = 5{\cdot}9 \times 10^{-9}$ kg.$^{-2}$ mole^2.
Curve *C*. (○) Corrected, by using $\chi_h = 23{\cdot}6 \times 10^{-9}$ kg.$^{-2}$ mole^2.
Curve *D*. (□) Corrected, by using $\chi_h = 35{\cdot}4 \times 10^{-9}$ kg.$^{-2}$ mole^2.

covered by reactions (1) and (2). Clearly the " hydrolysis correction " must include an adjustment made necessary by other, unknown, side reactions. The best straight line was calculated from the method of averages for the data represented by curve *D* and the slope gave $\chi_{3,5} = 1{\cdot}50$ kg. mole^{-1}. Each experimental point was then used to calculate a separate value of χ_3. From the resulting ten values a mean of 16·85 kg. mole^{-1} with a standard deviation of the mean of 0·09 was calculated. Hence $\chi_5 = 25{\cdot}3$ kg.^{2} mole^{-2}. For the present purpose it is not

TABLE 1. *Determination of* χ_3 *at* 25°. *All concentrations are molal* × 10^3. *Units of* χ_3 *are kg. of solvent mole*$^{-1}$.

$[Br_2^F]^*$	$[Br_2^F]$	$[Br_2^T]$	$[Br_2^C]$	$[Br_5^-]$	$[Br_3^-]$	$[BrO^-]$	$[Br_T^-]$	$[Br_F^-]$	χ_3
67·53	66·78	76·04	9·26	0·773	7·71	8·49	15·37	6·88	16·78
62·71	61·99	76·70	14·71	1·153	12·40	13·56	25·58	12·02	16·64
57·21	56·53	79·06	22·53	1·634	19·26	20·90	41·03	20·13	16·93
51·45	50·81	77·33	26·52	1·754	23·01	24·77	51·39	26·62	17·01
57·15	56·47	84·64	28·17	2·041	24·09	26·13	51·32	25·19	16·93
45·06	44·49	92·96	48·47	2·854	42·76	45·62	102·56	56·94	16·88
48·71	48·09	98·51	50·42	3·179	44·06	47·24	101·72	54·48	16·82
33·25	32·78	111·61	78·85	3·530	71·79	75·32	204·88	129·56	16·90
35·55	35·07	117·46	82·39	3·922	74·55	78·49	205·09	126·62	16·79
23·70	23·34	114·94	91·60	2·997	85·61	88·60	307·24	218·64	16·78
19·63	19·31	32·24	12·93	0·343	12·59	12·24	51·01	38·42	16·50
15·67	15·39	36·90	21·51	0·460	21·05	20·59	101·96	80·91	16·54
13·71	13·45	42·25	28·80	0·541	28·26	27·72	152·91	124·65	16·53
10·91	10·68	42·16	31·48	0·473	31·01	30·53	203·90	172·89	16·53

necessary to know $\chi_{3,5}$ with great accuracy; the above figure is probably not more than 2% in error. Some experiments at lower total bromine concentrations gave the results shown at the bottom of Table 1; a similar " hydrolysis correction " was needed for these also. For these four experiments $\chi_{3,5}$ was found to be 1·45 kg. mole^{-1} and the mean value of $\chi_3 = 16{\cdot}53$ kg. mole^{-1}. This small but definite difference has not yet been explained, and in the

TABLE 2. χ_3 *at* 35°. *All concentrations are molal* × 10^3. *Units of* χ_3 *are kg. of solvent mole*$^{-1}$.

$[Br_3^F]$*	$[Br_3^F]$	$[Br_3^T]$	$[Br_3^O]$	$[Br_5^-]$	$[Br_3^-]$	$[Br_O^-]$	$[Br_T^-]$	$[Br_F^-]$	χ_3
27·02	26·62	120·28	93·66	3·032	87·60	90·63	305·79	215·16	15·29
27·04	26·64	120·72	94·08	3·047	87·99	91·03	305·18	214·15	15·42
38·43	37·92	118·16	80·24	3·601	73·04	76·64	203·85	127·21	15·14
37·12	36·62	115·23	78·61	3·417	71·78	75·19	203·73	128·54	15·25
49·05	48·43	96·06	47·63	2·663	42·30	44·97	101·99	57·02	15·32
58·35	57·66	84·14	26·48	1·726	23·03	24·75	51·06	26·31	15·18
58·49	57·80	79·05	21·25	1·388	18·47	19·86	40·79	20·93	15·27
61·27	60·56	82·39	21·83	1·485	18·86	20·34	40·77	20·43	15·24
58·14	57·45	70·75	13·30	0·864	11·57	12·44	25·54	13·10	15·37

TABLE 3. χ_3 *at* 5°. *All concentrations are molal* × 10^3. *Units of* χ_3 *are kg. of solvent mole*$^{-1}$.

$[Br_3^F]$*	$[Br_3^F]$	$[Br_3^T]$	$[Br_3^O]$	$[Br_5^-]$	$[Br_3^-]$	$[Br_O^-]$	$[Br_T^-]$	$[Br_F^-]$	χ_3
23·86	23·72	93·94	70·22	2·958	64·30	67·26	203·82	136·56	19·85
36·07	35·87	106·43	70·56	4·310	61·94	66·25	152·84	86·59	19·94
35·51	35·31	81·67	46·36	2·793	40·77	43·57	102·01	58·44	19·76
51·30	51·05	80·33	29·28	2·420	24·44	26·86	51·02	24·16	19·82
51·13	50·88	80·06	29·18	2·406	24·37	26·77	50·94	24·17	19·82
58·61	58·33	74·20	15·87	1·464	12·94	14·41	25·54	11·13	19·93

subsequent calculations on the equilibria in the mercuric bromide–bromide ion system the value of χ_3 and of $\chi_{3,5}$ appropriate to the range of bromine concentration employed was used. This avoided the difficulty in the only simple manner which was possible.

(ii) At 35°.—The same " hydrolysis correction " was necessary, and the results are displayed in Table 2. From the corrected values a linear plot of α against β was obtained, and, from the slope, a value of $\chi_{3,5} = 1{\cdot}30$ kg. mole^{-1}. The mean of nine separate estimates of χ_3, obtained as described earlier, was 15·28 kg. mole^{-1}, standard deviation of the mean 0·08.

(iii) At 5°.—A lower " hydrolysis constant " of $5{\cdot}9 \times 10^{-9}$ kg.$^{-2}$ mole^2 was required to give a linear plot of α against β, when the data of Table 3 were used. This compares with the value $\chi_h = 0{\cdot}57 \times 10^{-9}$ kg.$^{-2}$ mole^2 found by Jones and Hartmann.[4] From the slope of this plot $\chi_{3,5} = 1{\cdot}94$ kg. mole^{-1}. The six calculated values of χ_3 gave a mean of 19·85 kg. mole^{-1}, standard deviation 0·07.

DISCUSSION

The reproducibility of the results compares favourably with the best previous work. The only extensive series previously reported at constant salt concentration was that due to Griffith, McKeown, and Winn [4] who used a liquid-phase partition method and applied a correction for the activity coefficient of bromine. Six determinations in 0·1 molar potassium bromide over a bromine concentration range 5—46 mmoles l.$^{-1}$ gave a mean $\chi_3 = 17{\cdot}40$ l. mole^{-1}, and a standard deviation of the mean of 0·05 at 21·5°. Over a range of ionic strengths quite large variations in χ_3 have been observed, and there is in addition a small but definite effect due to the cation. For example, Jones and Baeckström [2] used the present method and, after correcting for the change in activity of the bromine, found χ_3 to vary between 15·5 and 19·3 as the potassium bromide content varied between 0·01 and 1·0 molar, and the bromine content from about 0·01 to 0·75 molar. On the whole their values increased with decreasing salt content; this was not found by Griffiths, McKeown, and Winn,[4] who concluded that the constant increased with increasing ionic strength up to $I = 0{\cdot}3$—0·6, and then decreased again. Jones and Baeckström selected $\chi_3 = 16$ l. mole^{-1}, and $\chi_{3,5} = 2{\cdot}5$ l. mole^{-1} as the " best " values at 25°; these are as close to our present values (which are expressed in terms of molal concentrations) as can reasonably be expected, especially since these refer to solutions in which the ratio of bromine to bromide was higher than that used in either ref. 2 or 4. A selection of earlier values is shown in Table 4, from which the effects of temperature and of the cation used can be seen.

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The importance of using χ_3 values obtained under the experimental conditions which are to be used in any subsequent complex studies is clear from inspection of this Table.

TABLE 4. *Selected earlier values of* χ_3 (*l. mole*$^{-1}$).

Salt	Temp.	χ_3	Source	Salt	Temp.	χ_3	Source
KBr	0°	19·6	Jones and Hartmann [2]	NaBr (I = 0·5)	21·5°	16·6	ref. 4
				LiBr (I = 0·5)	21·5	16·2	,,
KBr (I = 0·5)	16·5	18·2	ref. 4	KBr	25·0	16·1	ref. 3, calc. by Lewis and Storch [8]
NaBr (I = 0·5)	16·5	17·4	,,				
KBr (I = 0·5)	21·5	17·4 (mean of two)	,,	KBr	32·5	15·4	ref. 1

Thermodynamic constants for the reaction between bromine and a bromide ion to form the tribromide ion when reactants and products are at unit mole fraction can be obtained without serious error from the experimental equilibrium constants (see following paper). ΔG_3° proves to be almost independent of temperature; at 278° K it is −1650 cal. mole^{-1}, at 298° K, −1670 cal. mole^{-1}, and at 308° K, −1670 cal. mole^{-1} also. Thus the entropy change during the addition of the bromide ion to the bromine molecule is very small (~0) and comparable with that for the formation of the tri-iodide ion from iodine and an iodide ion. This can be calculated to be about −1·5 cal. mole^{-1} deg.$^{-1}$ from Jones and Kaplan's data,[9] who measured χ_3 at 0° and 25°. The possibility of serious error in this kind of calculation is however well shown by comparing this value with the much larger negative one (−5 cal. mole^{-1} deg.$^{-1}$) found in a recent extinctiometric study of the iodine–tri-iodide equilibrium [10] and the above value for ΔS_3° is not to be regarded as definitive.

SHEFFIELD UNIVERSITY. [*Received, May 29th*, 1957.]

[9] Jones and Kaplan, *J. Amer. Chem. Soc.*, 1928, **50**, 1845.
[10] Awtrey and Connick, *ibid.*, 1951, **73**, 1842.

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72. *Formation Constants of* $HgBr_3^-$ *and* $HgBr_4^{2-}$ *at 5°, 25°, and 35° in Aqueous Medium of Constant Ionic Strength and Acidity.*

By D. B. SCAIFE and H. J. V. TYRRELL.

The formation constants of the ions $HgBr_3^-$ and $HgBr_4^{2-}$ have been measured at 5°, 25°, and 35° over a wide range of free bromide concentrations by a new method in which bromine and mercuric bromide compete for bromide ions. The results at 25° have been confirmed at low free bromide-ion concentrations through the absorption spectra of the solutions containing the complex ions. The constants obtained at this temperature differ slightly from the earlier values obtained over a limited and rather high range of free bromide-ion concentrations. Evidence for the formation of a weak donor–acceptor complex $HgBr_6^{2-}$ from $HgBr_4^{2-}$ and Br_2 has been obtained. The thermodynamic constants for the formation of $HgBr_3^-$ and of $HgBr_4^{2-}$ have been estimated from the measured formation constants.

AQUEOUS solutions of the sparingly soluble mercuric halides contain principally the undissociated HgX_2 molecules (X = Cl, Br, I), a small proportion of HgX^+, and negligible amounts of Hg^{2+}. In the presence of excess of halogen ions, the solubility of the mercuric halide is greatly increased; it is generally agreed that this enhanced solubility is due to the formation of the complex anions HgX_3^- and HgX_4^{2-}. Thus the species HgX^+, HgX_2, HgX_3^-, HgX_4^{2-} form a set of successive co-ordination complexes of Hg^{2+} with X^- as the co-ordinating group. The equilibria involved in the formation of these complexes have frequently been studied, most recently by Sillén and his associates [1–6]; the addition of

the first two halogen anions to the mercuric ion takes place with great ease, the complexes HgX^+ and HgX_2 being very stable. On the other hand, the higher complexes HgX_3^-, HgX_4^{2-} are much less stable, and this might suggest that two of the ligand groups in HgX_4^{2-} are held more firmly than the rest. However, the most recent evidence, from Raman spectra,[9,10] suggests that all four bonds in HgX_4^{2-} are equivalent, and that the ion is tetrahedral. A pyramidal configuration has been suggested [9] for the ion HgX_3^-, though it is equally possible to interpret the spectroscopic evidence in terms of a tetrahedral configuration, the vacant co-ordination position being occupied by a water molecule.[10] In any event, the addition of further X^- ions to HgX_2 involves, according to this evidence, a fundamental change in structure.

The only modern study of the equilibrium constants of the mercuric bromide–bromide ion system, by Bethge, Jonevall-Westöö, and Sillén,[6] was limited to one temperature (25°) and to rather high free bromide-ion concentrations, and the constants were obtained indirectly by combining the results of several electrometric titrations. A direct electrometric determination of the free bromide-ion concentration does not seem to be easy, and the method developed in the preceding paper of using bromine as indicator has been used here. The ionic strength and acidity ($I = 0{\cdot}5$; pH = 2) of the solutions were maintained constant at approximately † the values used by Sillén *et al.*[1-8] by adding sodium perchlorate and perchloric acid, and experiments were carried out at 5°, 25°, and 35°. At low free bromide-ion concentrations the observations at 25° were supplemented by a study of the light absorption at λ 310 mμ.

The great difference in stability between HgX_2 and the anions HgX_3^- and HgX_4^{2-} makes it possible to study their formation constants as if HgX_2 were the central group, *i.e.*, the ionisation of HgX_2 can be neglected in the presence of even small amounts of free X^-. In the following discussion therefore it is assumed that only the following equilibria need be considered:

$$HgBr_2 + Br^- \rightleftharpoons HgBr_3^- : K_{2,3} \equiv [HgBr_3^-]/[HgBr_2][Br^-]$$
$$HgBr_3^- + Br^- \rightleftharpoons HgBr_4^{2-} : K_{3,4} \equiv [HgBr_4^{2-}]/[HgBr_3^-][Br^-]$$

The earlier workers used χ_3 instead of $K_{2,3}$ and χ_4 for the product $K_{2,3}.K_{3,4}$; the present notation has been adopted to provide a logical set applicable to each successive stage in the complex formation.

Experimental

(i) *Bromine Indicator Method.*—The procedure was that described in the preceding paper for the bromine–bromide ion system except that a known quantity of pure mercuric bromide was added to the solution containing the sodium bromide. Hydrolysis corrections were made to all measured values of $[Br_2^F]^*$ by use of the correction terms used for the bromine–bromide ion system at the appropriate temperature. There is a slight additional complication in the calculation since the total combined bromide ($[^TBr_C^-]$) is now made up of the bromide combined with the mercuric bromide ($[^mBr_C^-] = C_L - [L]$ where [L] represents the free ligand concentration, and C_L is the total concentration of ligand available for combination with the mercuric bromide present) and that combined with the bromine ($[^bBr_C^-]$). Eqns. (1)—(3), in the notation

† In the bromine indicator method it was convenient to use a molal rather than a molar scale of concentration, and both ionic strengths and acidities have been calculated on this basis. The conditions used were not therefore quite the same as those used by Sillén *et al.*

1 Sillén, *Svensk kem. Tidskr.*, 1946, **58**, 52.
2 Sillén and Infelt, *ibid.*, p. 61.
3 Jonsson, Qvarfort, and Sillén, *Acta Chem. Scand.*, 1947, **1**, 461.
4 Sillén, *ibid.*, p. 473.
5 Lindgren, Jonsson, and Sillén, *ibid.*, 1948, **1**, 479.
6 Bethge, Jonevall-Westöö, and Sillén, *ibid.*, 1948, **2**, 828.
7 Qvarfort and Sillén, *ibid.*, 1949, **3**, 505.
8 Sillén, *ibid.*, p. 539.
9 Delwaulle, François, and Wiemann, *Compt. rend.*, 1938, **206**, 1108; **207**, 340.
10 Rolfe, Sheppard, and Woodward, *Trans. Faraday Soc.*, 1954, **50**, 1275.

of the preceding paper, hold. From the experimental measurements, and the known constant for the formation of the pentabromide anion ($\chi_{3,5}$), $[Br_5^-]$ was calculated as before. $[Br_3^-]$ was then obtained from eqn. (4) of the preceding paper, and used with values of $[Br_2^F]$ and χ_3

$$[^TBr_C^-] = [^bBr_C^-] + [^mBr_C^-] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$[^bBr_C^-] = [Br_2^C] - [Br_5^-] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

cf. eqn. (6) of preceding paper.

$$[Br_F^-] = [Br_T^-] - [^TBr_C^-] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

to determine $[Br_F^-]$. The quantity $[^mBr_C^-]$ was then obtained from eqns. (1)—(3). The average ligand number $\bar{n} = [^mBr_C^-]/C_M$. Each experiment gave a single value of $\bar{n}$ and the corresponding value of $[Br_F^-]$.

(ii) *Spectroscopic Method.*—For a solution of optical density D in a cell d cm. long, a mean extinction coefficient ε_M can be defined by the relation,

$$D = \varepsilon_M \,.\, C_M \,.\, d$$

where C_M is the total concentration of the central group. If there are only mononuclear complexes present the mean extinction coefficient is a function of the free ligand concentration only.[11–13] Thus, solutions having the same value of ε_M must have the same value of [L] (" corresponding solutions "), and hence of $\bar{n}$. In order to minimise instrumental errors, Ahrland's technique [11] of working at a constant optical density was used; this method requires the use of at least two, and preferably more, absorption cells of accurately known length maintained at constant temperature. A modified Beckman DU spectrophotometer was used, and the design of the cells and their method of calibration are described elsewhere.[14] The ultraviolet absorption curve of mercuric bromide consists of a steep absorption step in the region 290—330 mμ, below which light transmission is negligible, and above which it is almost complete. There is, therefore, little latitude in the choice of wavelength. The constant optical density to be used was selected in the region of maximum sensitivity to concentration changes, namely $D = 0{\cdot}65$, and a wavelength of 310 mμ chosen to suit the available cells and the concentration range of mercuric bromide. At this wavelength, solutions of sodium bromide, sodium perchlorate, and perchloric acid are completely transparent. In addition, the absorption curve of mercuric bromide was not affected by the addition of perchlorates, suggesting that no complex formation occurs between mercuric bromide and perchlorate anions. Hence the solutions could safely be " loaded " with perchloric acid and sodium perchlorate to the acidity (0·01 molar) and ionic strength ($I = 0{\cdot}5$ on the molar scale) required. The molar scale was used instead of the molal scale used in the bromine indicator method. Pairs of solutions were prepared as follows: (*a*) C_L mmoles l.$^{-1}$ of sodium bromide, 10 mmoles l.$^{-1}$ of perchloric acid, and sodium perchlorate to $I = 0{\cdot}5$; (*b*) C_L mmoles l.$^{-1}$ of sodium bromide, 10 mmoles l.$^{-1}$ of perchloric acid, 15 mmoles l.$^{-1}$ of mercuric bromide, and sodium perchlorate to $I = 0{\cdot}5$, where $C_L = 20$, 15, 12, 10, 8, 6, and 4.

For each value of C_L, solutions (*a*) and (*b*) were mixed in the proportions to give the required optical density when placed in cells 0·5 cm., 1·0 cm., and 2·0 cm. long. An optical density of 0·65 could not be attained in the 0·5 cm. cell when $C_L = 6$ or 4 by mixing the above solutions, owing to the low concentration of mercuric bromide in (*b*) which could not be increased further because of the low solubility of mercuric bromide in the presence of such small quantities of excess of bromide. The omission of these readings did not affect the results seriously. It follows from the Beer–Lambert law that, for a given cell length, log ε_M should be linear with log C_M. It is therefore simple to obtain interpolated values of C_M corresponding to arbitrary values of ε_M. There is no simple relation between ε_M and C_L, corresponding values of these two quantities falling on a smooth curve, but it has been said [11] that a plot of ε_M/C_L against C_L is more nearly linear and therefore more suitable for interpolation. This was not so for the present results, so the simple plot of ε_M against C_L was used to obtain values of C_L corresponding to the arbitrarily selected values of ε_M. By this means, pairs of C_M, C_L values corresponding

[11] Ahrland, *Acta Chem. Scand.*, 1949, **3**, 783.
[12] Olerup, Dissertation, Lund, 1944; quoted in ref. 11.
[13] Fronaeus, Dissertation, Lund, 1948; quoted in ref. 11.
[14] Richards, Scaife, and Tyrrell, to be published.

to a given ε_M were obtained, one pair for each cell length. If only mononuclear complexes are present, for solutions having the same ε_M value, C_M should be a linear function of C_L, though the fact that this is so does not entirely exclude the existence of polynuclear complexes. The slope of the line is equal to the average ligand number corresponding to the particular value of ε_M, and the intercept at $C_M = 0$ to the free ligand concentration [L].[15]

(iii) *Preparation of Materials.*—Mercuric bromide was purified by two successive sublimations of B.D.H. Laboratory Reagent Grade material. The other chemicals were purified as described in the preceding paper.

TABLE 1. *The system* $HgBr_2$–Br^- *at* 25° (*bromine indicator method*). *All concentrations are molal* × 10^3. *The sign* † *shows that the experiment was not used in the calculation of the formation constants.*

Expt.	$[Br_2^F]$*	$[Br_2^F]$	$[Br_2^T]$	$[Br_F^-]$	$[Br_T^-]$	C_M	$p[Br_F^-]$	$\bar{n}$
1 †	23·97	23·60	105·76	193·23	305·81	20·50	0·714	1·617
2 †	30·04	29·60	128·36	181·65	309·64	20·87	0·741	1·596
3 †	35·41	34·93	104·75	107·37	206·62	20·98	0·969	1·561
4 †	44·96	44·39	102·63	68·72	154·90	20·68	1·163	1·516
5	45·70	45·12	92·39	54·76	129·02	20·51	1·261	1·453
6	49·06	48·44	85·99	40·17	103·30	20·63	1·396	1·355
7	50·71	50·08	88·05	39·12	102·67	20·93	1·408	1·341
8	52·58	51·93	85·19	32·89	89·79	20·56	1·483	1·259
9	59·43	58·73	91·23	27·92	82·51	20·60	1·554	1·190
10	61·76	61·05	94·55	27·52	82·60	20·63	1·560	1·167
11	64·41	63·68	90·84	21·25	77·53	29·04	1·673	1·078
12	65·66	64·93	84·77	15·18	51·78	20·24	1·819	0·908
13	63·32	62·60	76·98	11·49	41·36	20·64	1·940	0·817
14	68·41	67·66	79·91	8·93	30·90	15·11	2·049	0·711
15	62·65	61·93	73·59	9·42	30·78	15·25	2·026	0·696
16	67·23	66·49	76·18	7·21	25·80	15·32	2·142	0·634
17	64·32	63·59	72·44	6·93	23·65	14·96	2·159	0·573
18 †	10·64	10·41	36·21	145·51	203·86	20·33	0·837	1·620
19 †	12·44	12·20	33·17	100·41	152·91	20·26	0·998	1·574
20 †	15·51	15·23	35·33	76·46	127·42	20·25	1·117	1·545
21	16·81	16·52	32·61	56·24	102·04	20·38	1·250	1·476
22	18·42	18·12	30·05	37·83	76·55	20·27	1·422	1·336
23	19·52	19·20	26·36	21·36	51·07	20·49	1·668	1·110
24 †	29·10	28·67	112·76	160·28	304·11	40·51	0·795	1·557
25 †	29·48	29·05	113·15	158·04	305·42	42·70	0·801	1·561
26 †	14·12	13·86	40·95	113·66	203·39	40·11	0·944	1·575
27	14·98	14·71	36·40	78·47	152·91	36·04	1·105	1·525
28	19·59	19·27	27·46	24·36	76·48	40·33	1·613	1·095

RESULTS

(i) *Bromine Indicator Method.*—As important conclusions can be drawn from the investigation at 25°, the results at this temperature are considered first (Table 1). The series 1—17 was done with an approximately constant total amount of bromine ($[Br_2^F] + [Br_2^T]$) in the system, and by assuming $\chi_3 = 16{\cdot}85$ kg. mole^{-1}, and $\chi_{3,5} = 1{\cdot}50$ kg. mole^{-1} in the calculations. The total mercuric bromide concentration was also kept constant in most of the experiments at about 20 mmoles per 1000 g. of solvent. When the free bromide was relatively low, C_M was changed within the range 15—40 mmoles per 1000 g. of solvent without noticeable effect on the experimental formation curve. This is a necessary condition for the conclusion that only mononuclear complexes exist. A preliminary calculation of the constants of the system was attempted by plotting $\bar{n}/\{(\bar{n} - 1) . [L]\}$ against $(2 - \bar{n}) . [L]/(\bar{n} - 1)$.[16,17] The expected linear relation for a system containing only mononuclear complexes was found between these two functions, except for the three points corresponding to experiments 1, 2, and 3 (Table 1) which lay far from the main line (Fig. 1). A set of temporary constants was calculated from the best straight line (calculated by "least squares") through the remaining points, and the values used to calculate a formation curve. Points 1—3 lay below this curve, the deviations increasing as $p[Br_F^-]$

[15] J. Bjerrum, "Metal Ammine Formation," P. Haase and Son, Copenhagen, 1941.
[16] F. J. C. Rossotti and H. S. Rossotti, *Acta Chem. Scand.*, 1955, **9**, 1166.
[17] Irving and H. S. Rossotti, *J.*, 1953, 3397.

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decreased, as illustrated in Fig. 2 where, however, the calculated formation curve has been obtained from the values of the association constants found by the methods described below, only the experimental points found at values of $p[Br_F^-] > 1{\cdot}2$ being used. This was the value below which the experimental points diverged from the preliminary formation curve calculated from the temporary set of constants. When $p[Br_F^-]$ was less than 1·2, the effect of changing either the bromine content or the mercuric bromide concentration was both noticeable and reproducible. A decrease in the total bromine in the system (using $\chi_3 = 16{\cdot}53$ kg. mole^{-1} and $\chi_{3,5} = 1{\cdot}45$ kg. mole^{-1}, the appropriate constants for

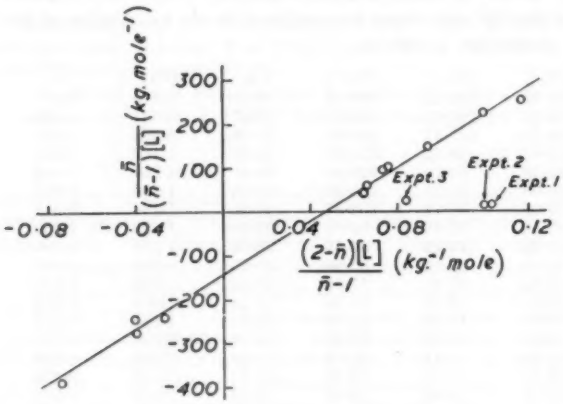
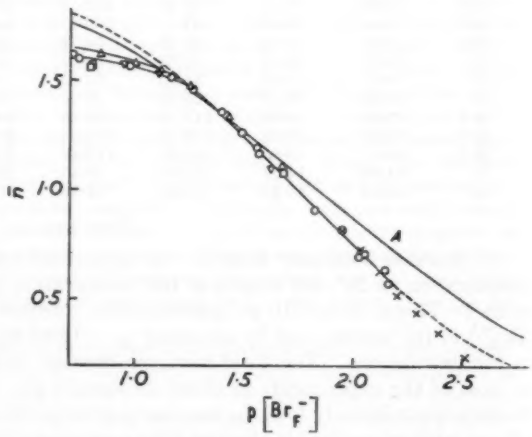


FIG. 1. *Preliminary calculation of formation constants at 25° by graphical method of Rossotti and Rossotti.*[16]

FIG. 2. *Formation curves at 25°.*

○ High bromine content.
□ ,, ,, (high C_M).
△ Low ,, ,,
▽ ,, ,, (high C_M).
× Spectroscopic data.

The full curves through the experimental points are apparent formation curves. The broken extensions at each end are obtained from formation constants calculated from experimental data obtained when $p(Br_F^-) > 1{\cdot}2$. The curve calculated from Sillén's [6] formation constants is also shown as a full line, *A*.



the bromine concentration range used; see preceding paper) increased the apparent $\bar{n}$ value, while an increase in mercuric bromide concentration decreased it. Between $p[Br_F^-] = 1{\cdot}2$ and 1·7 such changes had no definite effect on the results; the reproducibility near 1·7 was slightly less satisfactory than at lower values because a decrease in the bromine and an increase in the mercuric bromide concentration both tend to reduce the quantity $[Br_2^0]$. This is measured by difference, and the analytical errors become more important as $[Br_2^F]$ approaches $[Br_2^T]$. When $p[Br_F^-] > 1{\cdot}7$, it was not practicable to study the effect of changes in bromine or total mercuric bromide concentrations for this reason. However, the independent spectroscopic data fall quite closely on the extrapolated formation curve (Fig. 2), and confirm its general accuracy. It is reasonable to conclude that the deviations are only important for values of $p[Br_F^-]$ below 1·2.

The simplest explanation of these is that bromine forms donor–acceptor complexes with either $HgBr_3^-$ or $HgBr_4^{2-}$ or with both, according to the following equilibria:

$$HgBr_3^- + Br_2 \rightleftharpoons HgBr_5^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

$$HgBr_4^{2-} + Br_2 \rightleftharpoons HgBr_6^{2-} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

The following symbolism is adopted: $m_n \equiv [HgBr_n]$, irrespective of charge; $b_n \equiv [Br_n]$, irrespective of charge; $a \equiv$ true free bromide concentration; $a' \equiv$ apparent free bromide concentration calculated without regard to the possible formation of $HgBr_5^-$ and $HgBr_6^{2-}$. Equilibrium constants (χ_3, $\chi_{3,5}$, $K_{2,3}$, $K_{3,4}$), defined in this and in the preceding paper, can be expressed in terms of this symbolism, as can the constants for the reactions (3) and (4), thus:

$$K_5 \equiv [HgBr_5^-]/[HgBr_3^-][Br_2] \equiv m_5/m_3b_2$$

$$K_6 \equiv [HgBr_6^{2-}]/[HgBr_4^{2-}][Br_2] \equiv m_6/m_4b_2$$

Using the method of calculation outlined above, which omits equilibria (3) and (4), we obtain an apparent average ligand number $\bar{n}$, and the apparent free bromide-ion concentration a' instead of the true values $\bar{n}_0$ and a respectively. It can be shown that, if equilibria (3) and (4) are included,

$$a' = a + (m_5 + m_6)/(1 + 2\chi_{3,5}b_2)\,\chi_3 b_2$$

Hence $a' \geqslant a$, and $p[a'] \leqslant [a]$. The difference will not be large if m_5 and m_6 are small, and the difference between $p[a']$ and $p[a]$ will be even smaller. Again, it can be shown that,

$$\Delta\bar{n} \equiv (\bar{n} - \bar{n}_0) = \{m_6 - (m_5 + m_6)(\bar{n}_0 + \theta - 1)\}/C_M$$

where

$$\theta = \frac{1 + \chi_3 b_2(1 + \chi_{3,5}\,b_2)}{\chi_3 b_2(1 + 2\chi_{3,5}\,b_2)}$$

As can be seen, θ is a function only of the known constants of the bromine–bromide system, and of the free bromine concentration; it can therefore be calculated unequivocally. Now $\Delta\bar{n}$ is negative if

$$\bar{n}_0 + \theta - 1 > m_6/(m_5 + m_6)$$

Provided that $\theta > 2 - \bar{n}_0$, this inequality holds for all values of m_5 and m_6. In the present work, $(2 - \bar{n}_0)$ could be calculated from the extrapolated formation curve of Fig. 2, and θ was found always to be in excess of this quantity. Hence the observation that $\Delta\bar{n}$ was negative in the region where deviations were observed is consistent with the hypothesis that reactions (3) and (4) take part in the complex equilibria when bromide ions are in excess. It can be seen that

$$m_6 = K_{2,3}K_{3,4}K_6 m_2 a^2 b_2$$

$$m_5 = K_{2,3}K_5 m_2 a b_2$$

Hence

$$\Delta\bar{n} = \frac{K_{2,3}ab_2[K_{3,4}K_6 a - (K_{3,4}K_6 a + K_5)(\bar{n}_0 + \theta - 1)}{1 + K_{2,3}a(1 + K_{3,4}a + K_5 b_2 + K_{3,4}K_6 a b_2)} \quad . \quad . \quad . \quad (5)$$

If it is assumed that a' is a good approximation to a, $\bar{n}_0$ corresponding to a particular value of a can be obtained either by extrapolation from the formation curve of Fig. 1, or by an equivalent procedure from the equation,

$$\bar{n}_0 = K_{2,3}a + 2K_{2,3}K_{3,4}a^2/[(1 + K_{2,3}a + K_{2,3}K_{3,4}a^2)]$$

To use this, it is necessary to obtain $K_{2,3}$ and $K_{3,4}$ from experiments at relatively low free bromide concentrations. $\Delta\bar{n}$ can be got from $\bar{n}_0$ and the experimental $\bar{n}$ at the same free bromide concentration, and eqn. (5) then contains only two unknowns, K_5 and K_6. Data from experiments 1, 3, 25, 26 were used to obtain four equations of the form (5), and all

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TABLE 2. *Calculated formation constants for the hypothetical complex ions* $HgBr_5^-$ *and* $HgBr_6^{2-}$ *at 25°.*

K_5 (kg. mole^{-1}) assuming $K_6 = 0$	10·8	9·5	3·7	5·3
K_6 (kg. mole^{-1}) assuming $K_5 = 0$	3·3	3·8	2·3	2·5

TABLE 3. *The system at 35° (bromine indicator method). All concentrations are molal* $\times 10^3$. *The sign † indicates that the experiment was not used for the calculation of the formation constants.*

Expt.	$[Br_2^F]$*	$[Br_2^F]$	$[Br_2^T]$	$[Br_F^-]$	$[Br_T^-]$	C_M	$p[Br_F^-]$	$\bar{n}$
1 †	28·36	27·94	114·22	188·54	302·72	20·60	0·725	1·496
2 †	38·54	38·03	87·01	76·75	152·94	20·32	1·115	1·447
3 †	43·23	42·66	85·15	58·72	127·50	20·37	1·231	1·395
4	48·43	47·82	82·91	43·20	101·91	20·36	1·364	1·259
5	48·36	47·75	77·31	36·07	88·74	20·38	1·443	1·214
6	50·35	49·72	77·30	32·14	81·61	20·34	1·493	1·154
7	55·30	54·63	84·51	31·29	81·35	19·87	1·505	1·110
8	58·36	57·67	83·29	25·28	71·37	20·43	1·597	1·084
9	59·89	59·19	85·29	25·01	69·90	19·60	1·602	1·047
10	53·04	52·39	72·17	21·75	61·18	20·44	1·662	1·020
11	60·56	59·86	82·05	20·99	61·19	20·33	1·678	0·959
12	59·47	58·77	76·42	17·05	51·05	20·34	1·768	0·862
13	59·07	58·38	72·06	13·32	40·77	20·38	1·875	0·720
14	61·60	60·89	74·48	12·61	40·72	20·32	1·899	0·760
15	63·14	62·42	75·97	12·22	40·81	20·45	1·913	0·782

TABLE 4. *The system at 5° (bromine indicator method). All concentrations are molal* $\times 10^3$. *The sign † indicates that the experiment was not used for the calculation of the formation constants.*

Expt.	$[Br_2^F]$*	$[Br_2^F]$	$[Br_2^T]$	$[Br_F^-]$	$[Br_T^-]$	C_M	$p[Br_F^-]$	$\bar{n}$
1 †	23·08	22·94	115·26	186·18	305·86	20·14	0·730	1·546
2 †	32·58	32·39	106·08	101·83	202·64	20·11	0·992	1·553
3 †	43·76	43·53	94·51	50·47	127·40	20·41	1·297	1·452
4	50·42	50·17	92·63	35·69	101·81	19·70	1·447	1·377
5	54·98	54·72	85·48	23·36	76·52	20·08	1·631	1·250
6	59·90	59·62	84·40	17·00	61·17	20·17	1·770	1·077
7	61·62	61·34	80·66	12·82	50·94	20·41	1·892	1·012
8	55·72	55·45	68·89	10·05	40·83	20·38	1·998	0·909
9	59·20	58·92	68·03	6·34	25·44	15·55	2·198	0·697

six possible solutions of these equations taken in pairs were obtained. Every estimate of K_6 was positive, but five out of six estimates of K_5 were negative. This suggests that it is incorrect to assume the simultaneous formation of both $HgBr_5^-$ and $HgBr_6^{2-}$. If K_6 is taken as zero, it is possible to estimate K_5 from eqn. (5) when no $HgBr_6^{2-}$ is present; similarly K_6 can be obtained by assuming K_5 to be zero. The resulting "constants" are shown in Table 2. From the much smaller variations of K_6 than of K_5, it seems more reasonable to assume that only $HgBr_6^{2-}$ is present; this would be expected for a donor–acceptor complex of the kind suggested. Although the estimate of K_6 as about 3 kg. mole^{-1} cannot be very accurate because of uncertainties in $\Delta\bar{n}$, it must be of the correct order of magnitude, if, as seems likely, the general explanation of the deviations given here is correct. Similar deviations at low $p[Br_F^-]$ values were observed at 5° and 35° but were not examined in detail. The full experimental results at these temperatures are given in Tables 3 and 4. The appropriate hydrolysis corrections were applied as described in the preceding paper.

(ii) *Spectroscopic Method (25° only).*—Figs. 3 and 4 show the variation of log ϵ_M with log C_M, and of ϵ_M with C_L respectively, for the three cells used. These had previously been calibrated as described elsewhere [14] in terms of the 0·5 cm. cell as a standard, by use of potassium nitrate solutions. Corresponding values of C_M and C_L at constant ϵ_M, interpolated from these graphs, are shown in Table 5, together with the derived $[Br_F^-]$ and $\bar{n}$ pairs. The plots of C_L against C_M at constant ϵ_M from which these were derived were

linear, as expected if polynuclear complexes were absent. This is not however a particularly sensitive test for the detection of small quantities of polynuclear complexes, but further investigation, at other wavelengths, was not practicable because of the unfavourable form of the absorption curve. Nor was it practicable to extend the experiments to higher free bromide concentrations; the variation of ε_M with increasing C_L became so small as

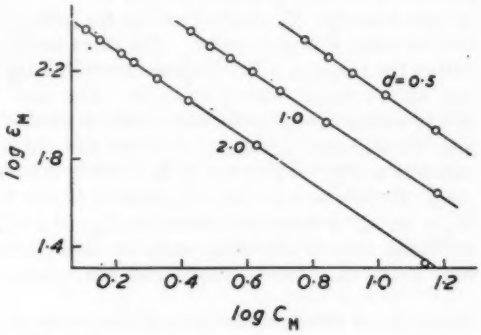

FIG. 3. log ε_M *as a function of* log C_M *at* 25° *at various values of* d *(cm.).*

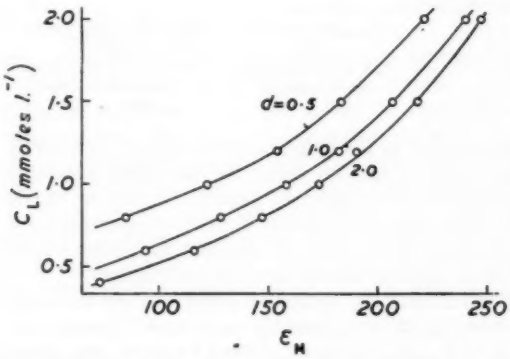

FIG. 4. C_L *as a function of* ε_M *at* 25°, *at various values of* d *(cm.).*

the maximum value of ε_M was approached that accurate interpolation in the C_L–ε_M curve became impossible. The experimental points are shown in Fig. 2 and agree well with those obtained by the other method.

TABLE 5. *Spectroscopic study of the system at* 25°. *All concentrations are molal* × 10^3 *(*d = *cell length).*

	d = 0·500 cm.		d = 0·997 cm.		d = 2·09 cm.			
ε_M	C_M	C_L	C_M	C_L	C_M	C_L	[L] = [Br_F^-]	$\bar{n}$
80	15·85	7·8	8·09	5·4	3·87	4·3	3·1	0·29
100	12·74	8·7	6·47	6·3	3·11	5·2	4·1	0·35
120	10·64	9·8	5·37	7·4	2·57	6·3	5·1	0·44
140	9·16	11·1	4·62	8·7	2·23	7·5	6·3	0·52
160	8·02	12·7	4·01	10·1	1·95	8·9	7·6	0·63
180	7·16	14·6	3·56	11·9	1·73	10·7	9·3	0·73
200	6·49	16·9	3·21	14·1	1·57	12·8	11·5	0·82

Calculation of the Complexity Constants.—There are many methods available, and the use of a graphical one for the bromine indicator data at 25° has already been mentioned. This is satisfactory except for values of $\bar{n}$ near unity where experimental errors become exaggerated. For a system in which only two successive complexes are formed

$$\bar{n} + (\bar{n} - 1)[Br_F^-]K_{2,3} + (\bar{n} - 2)[Br_F^-]^2 K_{2,3}K_{3,4} = 0 \quad . \quad . \quad . \quad (6)$$

There are two unknowns, and $K_{2,3}K_{3,4}$ could be obtained in principle from two points on the formation curve. However there are usually more data than the minimum, and the problem is to combine them. A general method would be to solve eqn. (5) by using all possible pairs of points in turn; this is laborious and points close together would be badly conditioned. Consequently, twelve experimental pairs of $(\bar{n},[Br_F^-])$ values were arranged in order of increasing $\bar{n}$, and the first and seventh, second and eighth, etc., pairs substituted in turn into eqn. (5), and solved for $K_{2,3}$, $K_{3,4}$. As before this general method is unsatisfactory when $\bar{n}$ is near unity. The third method used was based on the observation that, within the range of $p[Br_F^-]$ values for which the formation of $HgBr_6^{2-}$ can be neglected, $\bar{n}$ was almost linear with $p[Br_F^-](a)$. The best straight line through these experimental points was obtained by the least-squares method by assuming the error to lie entirely in n, and the standard deviation of $\bar{n}$ ($\sigma_{\bar{n}}$) calculated. Two points were selected at arbitrary values of a near the extreme ends of the true formation curve and assumed to be in error by $\pm\sigma_{\bar{n}}$. By solving eqn. (5) with pairs of points $(\bar{n}_1 + \sigma_{\bar{n}}, a)$, $(\bar{n}_2 - \sigma_{\bar{n}}, a_2)$, and $(\bar{n}_1 - \sigma_{\bar{n}}, a_1)$, $(\bar{n}_2 + \sigma_{\bar{n}}, a_2)$, a range of values for $K_{2,3}$ and $K_{3,4}$ was obtained from which an estimate of the mean, and of the likely, error of each constant could be calculated. Points near the ends of the calculated straight line were chosen partly because the true formation curve

TABLE 6. *Formation constants of the system at 25° calculated by different methods from the data in Table 1.*

Method	$K_{2,3}$ (kg. mole^{-1})	$K_{2,3}K_{3,4}$ (kg.^{2} mole^{-2})
Graphical, see refs. 16, 17	136	3030
Solution of pairs of simultaneous equations	139 with standard deviation 13	3050 with standard deviation 160
Linear approximation method	135 ± 10	3060 ± 200

should coincide most closely with the straight line at the ends and in the centre, and partly because the term $(n - 1)$ is then as large as possible. By using the calculated constants from these selected points the true formation curve could be found. It was so nearly linear in the region of $p[Br_F^-]$ used, that the standard deviation of the experimental $\bar{n}$ values from the least-squares line was identical with that from the true formation curve. This completely justifies the use of the linear approximation method for this case.

The results of the three methods of calculating the formation constants are shown in Table 6. The previous potentiometric study at 25° at almost the same ionic strength and acidity [6] gave $K_{2,3} = 260 \pm 70$ l. mole^{-1}, $K_{2,3}K_{3,4} = 4700 \pm 200$ l.^{2} mole^{-2}; the formation curve calculated from these figures is shown in Fig. 2.

The linear approximation method alone was used on the data obtained at 5° and 35°, since the experimental formation curves were substantially linear in the regions where there was no appreciable interaction between the competing complex systems. The values excluded from the calculations are indicated in Tables 3 and 4. It was found that the complexity constants had the following values: (*a*) at 5° $K_{2,3} = 230 \pm 25$ kg. mole^{-1}; $K_{2,3}K_{3,4} = 5900 \pm 600$ kg.^{2} mole^{-2}; (*b*) at 35° $K_{2,3} = 110 \pm 20$ kg. mole^{-1}; $K_{2,3}K_{3,4} = 2000 \pm 250$ kg.^{2} mole^{-2}. No attempt to calculate the constants K_5 or K_6 was made at these temperatures.

The results of the spectroscopic investigation at 25° were used to calculate complexity constants by the first method described above. A satisfactory straight line was obtained and gave the following constants: $K_{2,3} = 100$ l. mole^{-1}; $K_{2,3}K_{3,4} = 4000$ l.^{2} mole^{-2}. In view of the limited concentration range to which the observations were limited these values are not as satisfactory as those found by using the bromine indicator method.

Calculation of the Thermodynamic Functions of the System.—The thermodynamic complexity constants (K^T) are related to the experimental constants by the equations:

$$K_{2,3}{}^T = K_{2,3} \cdot \frac{\gamma_{HgBr_2}}{\gamma_{Br^-} \cdot \gamma_{HgBr_3^-}}; \quad K_{3,4}{}^T = K_{3,4} \cdot \frac{\gamma_{HgBr_4^{2-}}}{\gamma_{Br^-} \cdot \gamma_{HgBr_3^-}}$$

where γ are the activity coefficients on the molal scale.

If $\Delta G^{app.}$, $\Delta H^{app.}$, and $\Delta S^{app.}$ are the quantities obtained by the usual methods from the experimental constants and their variation with temperature, and $\Delta G°$, $\Delta H°$, and $\Delta S°$ are the corresponding changes for the hypothetical ideal reference system when products and reactants are at unit molality, it can be shown [18] that

$$\Delta G^{app.} = \Delta G° - \sum_i \nu_i \ln \gamma_i$$

$$\Delta H^{app.} = \Delta H° - RT^2 \sum_i \nu_i \, \partial/\partial T(\ln \gamma_i)$$

$$\Delta S^{app.} = \Delta S° - R[T \sum_i \nu_i \, \partial/\partial T(\ln \gamma_i) + \sum_i \nu_i \ln \gamma_i]$$

The quantities ν_i are the stoicheiometric coefficients of the components taking part in the reaction. In sufficiently dilute solution the activity coefficients could be calculated from an extended form of the Debye–Hückel equation, such as that [19] due to Davies, $-\log \gamma_i = Az_i^2\{[\sqrt{I}/(1 + \sqrt{I})] - 0{\cdot}2I\}$. Strictly, this is not valid at $I = 0{\cdot}5$ but will be used to obtain some idea of the corrections required for the deviations from ideal behaviour. The temperature coefficient of the activity coefficient can be estimated from the known variation in A with temperature, or by a method formerly suggested by one of us.[20] In either case the approximate relation $\partial/\partial T \ (\log \gamma_i) = 2 \times 10^{-3} \log \gamma_i$ is found to hold at room temperature. The constant A has, for this purpose, been assumed to vary with temperature in the same way as the corresponding coefficient of the Debye–Hückel equation.

The activity coefficient correction to $K_{2,3}$, and to the quantities derived therefrom, will, according to this, depend only on the activity coefficient of the neutral molecule $HgBr_2$. This is unlikely to be far from unity, and the apparent changes in the thermodynamic functions G, H, and S can be equated to the standard state changes without serious error. For $K_{3,4}$ the apparent entropy change exceeds the true standard state entropy change by about 2 entropy units; this correction is probably small in comparison with the errors involved in the calculation of entropy changes by this method.

When $\log K_{2,3}$ was plotted against $1/T$, a satisfactory straight line was obtained from the slope of which $\Delta H_3^{app.}$ was found to be $-4{\cdot}3$ kcal. mole^{-1}. $\Delta G_{2,3}^{app.}$ at 5°, 25°, and 35° can be calculated as $-3{\cdot}01$, $-2{\cdot}91$, and $-2{\cdot}86$ kcal. mole^{-1} respectively. From these figures $\Delta S_{2,3}^{app.}$ can be calculated to be -5 e.u. According to the above arguments,

$$\Delta S_{2,3}° = \Delta S_{2,3}^{app.} = -5 \text{ e.u.}$$

The plot of $\log (K_{2,3}K_{3,4})$ against the reciprocal of the temperature was not quite linear, but from the average slope the apparent heat content change for the overall reaction to form $HgBr_4^{2-}$ was found to be $-6{\cdot}2$ kcal. mole^{-1} and the corresponding entropy change to be between -4 and -5 e.u. The apparent entropy change for the reaction $HgBr_3^- + Br^- \longrightarrow HgBr_4^{2-}$ must therefore be close to zero. $\Delta S_{3,4}°$ is therefore assigned the value -2 e.u. In all these calculations the equilibrium constants used were those obtained from the formation curves by the linear approximation method.

Discussion

The measurements at 25° by the bromine indicator method were done in conditions differing from those used in the earlier potentiometric measurements only in that concentrations were expressed on a molal, rather than a molar scale. An approximate calculation, the density of the solutions being assumed to be about 1·05, shows that $K_{2,3}$ calculated on a molal scale should be about 0·95 of that calculated on a molar scale. The corresponding factor for $K_{2,3}K_{3,4}$ is about 0·90. The constants obtained in the earlier work [6] when converted to a molal basis using these constants are therefore appreciably larger than

[18] Prigogine and Defay, "Chemical Thermodynamics," trans. Everett, Longmans, Green and Co. Ltd., London, 1952.
[19] Davies, *J.*, 1938, 2093.
[20] Tyrrell and Hollis, *Trans. Faraday Soc.*, 1952, **48**, 893.

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those derived from the present measurements. The effect on the formation curve of the change in concentration scale is very small, and cannot account for the difference illustrated in Fig. 2. The curve calculated from the earlier results coincides with that derived from the present measurements where $\bar{n}$ is large and $p[Br_F^-]$ small. This is just the concentration range to which the potentiometric measurements were restricted, and the discrepancy between the two sets of constants is presumably due very largely to the fact that a wider range of free bromide concentrations has been studied in this work. The excellent agreement of the two formation curves near the upper end justifies the assumption that, for $p[Br_F^-] > 1{\cdot}2$, the bromine–bromide and mercuric bromide–bromide equilibria can be considered as independent. If this had not been so, these curves could not have coincided so well. At high $p[Br_F^-]$ values the spectroscopic measurements fall on or near the extrapolated formation curve, and the constants derived from these alone are close to, though not quite identical with, those obtained by the bromine indicator method. It can fairly be claimed that the constants given in Table 6 are the most satisfactory ones at present available * for 25°. No independent data are available at the other temperatures studied.

TABLE 7. *Standard entropies of mercuric bromide complexes (e.u.).*

Species	$HgBr_2$	$HgBr_3^-$	$HgBr_4^{2-}$
Observed entropy	41	55	75
Calculated entropy	30	61	39

The entropy of solution of undissociated mercuric bromide can be calculated without serious error from the heat of solution and the solubility of mercuric bromide in water. At 25° a saturated solution of mercuric bromide contains 0·609 g. per 100 g. of water.[21,22] Corrections for dissociation are negligible, and the activity coefficient of mercuric bromide in the saturated solution can be assumed to be unity. The standard Gibbs free energy change on solution can then be calculated to be +2·4 kcal. mole^{-1}. The heat of solution [23] to form a saturated solution is +3·4 kcal. mole^{-1}. Corrections for dissociation are again negligible, and the measured heat being assumed to be equal to the standard heat of solution, the standard entropy of solution at 25° is +3·5 e.u. Accepting Latimer's estimate of 37·2 e.u. for the entropy of solid mercuric bromide,[24] we find that the standard entropy of undissociated mercuric bromide in water is 41 e.u. From this and the observed entropy changes, standard entropies for the ions $HgBr_3^-$ and $HgBr_4^{2-}$ can be calculated. These are shown in Table 7 together with the values calculated by the empirical methods suggested by Cobble.[25]

There are several points of interest. For the neutral molecule the experimental value is appreciably greater than the calculated one. The first is more reasonable, since, from it and the known entropies of the aqueous mercuric (−5·4 e.u.) and bromide (19·25 e.u.) ions [26] the standard entropy change for the reaction,

$$Hg^{++}, aq. + 2\ Br^-, aq. \longrightarrow HgBr_2, aq.$$

can be calculated to be +8 e.u. From Cobble's figure, the unlikely value of −3 e.u. would be obtained. The experimental entropy of $HgBr_4^{2-}$ is much greater than the calculated one; a similar discrepancy has been noted by Cobble [25] between the calculated value and

* *Added, October 11th*, 1957.—The results of a liquid-phase partition study at 25° of the complexes have now appeared (Marcus, *Acta Chem. Scand.*, 1957, **11**, 599). The constants differ slightly both from the present results and from those of Sillén and his co-workers.

[21] Garrett, *J. Amer. Chem. Soc.*, 1939, **61**, 2744.
[22] Tyrrell and Richards, *J.*, 1953, 3812.
[23] Berthelot, see Landolt–Börnstein, *Physikalisch-Chemische Tabellen*, Hw. II, 1556.
[24] Latimer, "The Oxidation States of the Elements and their Potentials in Aqueous Solution," Prentice-Hall, Inc., New York, 2nd Edn., 1952.
[25] Cobble, *J. Chem. Phys.*, 1953, **21**, 1443, 1446.
[26] Powell and Latimer, *ibid.*, 1951, **19**, 1139.

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that quoted by Latimer [24] which was based on the older data of Sherrill. Whatever the reason for this difference, it is surprising to find that $HgBr_4^{2-}$ apparently has a larger entropy than the singly charged species $HgBr_3^-$. The difference is so great that it can scarcely be attributed entirely to experimental errors in the temperature coefficients of the formation constants. It can be reduced, though not changed in sign, if it is assumed that the singly charged ion has a water molecule co-ordinated in its inner co-ordination sphere. The formation reaction is then

$$HgBr_2 + Br^- + H_2O \longrightarrow Hg[Br_3,H_2O]^-$$

The entropy of liquid water being assumed to be 17 e.u., the standard entropy of the singly charged complex ion becomes 72 e.u. This improvement lends some support to the view that when mercuric bromide co-ordinates with a bromide ion the linear (*sp*) hybridisation in the neutral molecule changes directly to tetrahedral (sp^3) hybridisation, the vacant site being occupied by a water molecule. This was suggested by Woodward [10] on the basis of Raman-effect measurements.

One of us (D. B. S.) is indebted to the University of Sheffield for the award of an Ellison Fellowship.

SHEFFIELD UNIVERSITY. [*Received, May 20th,* 1957.]

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73. *Tracer Studies in Alcohols. Part III.* Intermediates in the Pinacol–Pinacone Rearrangement.*

By C. A. BUNTON, T. HADWICK, D. R. LLEWELLYN, and Y. POCKER.

The rate of the acid-catalysed rearrangement of pinacol to picacone is proportional to Hammett's acidity function, h_0. Pinacol, isolated after incomplete reaction, has partially exchanged its oxygen atoms with those of the solvent ^{18}O-containing water, and comparison between the relative rates of this exchange and of rearrangement can give information on the fate of the carbonium-ion intermediate. At low concentration of acid, *ca.* 70% of the carbonium ions are captured by the solvent water to regenerate pinacol enriched in ^{18}O. This proportion decreases with increasing acidity. The nature of the intermediates is discussed.

WE sought evidence on the mechanism of the pinacol–pinacone rearrangement, and in particular to determine the nature of the carbonium-ion intermediate,[1] choosing the simplest possible system, namely the sulphuric acid-catalysed rearrangement of pinacol in water. Preliminary details have been given elsewhere.[2]

The pinacol rearrangement is faster in deuterium oxide than in water,[3,4] so the slow step of the reaction must be the decomposition of the conjugate acid (I) formed in a rapid reversible step. There is much chemical evidence to show that the migration of the alkyl group is intramolecular,[1] and it seems likely that the necessary intermediate for rearrangements in water is a carbonium ion. An epoxide has been isolated from the partial rearrangement of benzopinacol in moist acetic acid,[5] and appears to be an intermediate under these conditions, but as an epoxide cannot be an intermediate in the rearrangement of some 1 : 2-diols in aqueous solvents [1,3,3a] its presence in this rearrangement is probably due to special properties of the system.

* Part II, *J.*, 1957, 3402.

[1] Ingold, "Structure and Mechanism in Organic Chemistry," G. Bell & Sons Ltd., London, 1953.
[2] Bunton, Hadwick, Llewellyn, and Pocker, *Chem. and Ind.*, 1956, 547.
[3] Ley and Vernon, *J.*, 1957, 2987, 3256; *Chem. and Ind.*, 1956, 146.
[3a] Meerburg, *Rec. Trav. chim.*, 1905, **24**, 131; 1909, **28**, 267, 270.
[4] Duncan and Lynn, *Austral. J. Chem.*, 1957, **10**, 1.
[5] Gebhart and Adams, *J. Amer. Chem. Soc.*, 1954, **76**, 3925.

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The evidence relevant to the rôle of the solvent comes largely from observations on the dependence of rate upon acid concentration. Uni- and bi-molecular acid-catalysed solvolyses can often be differentiated provided that the reaction is followed at a concentration of acid sufficiently high for the protonating power of the solution (as measured by the Hammett acidity function, h_0) to be greater than the stoicheiometric concentration of hydrogen ions, $[H_3O^+]$. By the Zucker–Hammett hypothesis [6] the rate of a unimolecular reaction should follow h_0 whereas that of a bimolecular reaction should follow $[H_3O^+]$.

This test has been applied to a number of pinacol–pinacone rearrangements, with benzopinacol in moist acetic acid,[5] and with aliphatic glycols in aqueous acids.[2,3,7] In all cases the rate of rearrangement has increased with a high power of the acid concentration, but has been closely proportional to the Hammett acidity function, h_0.

Kinetic evidence on the molecularity of a reaction does not necessarily reveal the detailed mechanism. The rate of disappearance of pinacol, for rearrangement in aqueous acid, is the same as the rate of formation of pinacolone,[7] * so the intermediate does not build up. The evidence on the rearrangement in water is consistent with the view that a carbonium ion is formed slowly from the conjugate acid of the glycol (I) and this then decomposes to the products. Strong confirmation is provided by a comparison of the products of rearrangement of 2-methylpropane-1 : 2-diol and its ethers with those of other reactions which go through a carbonium ion.[3]

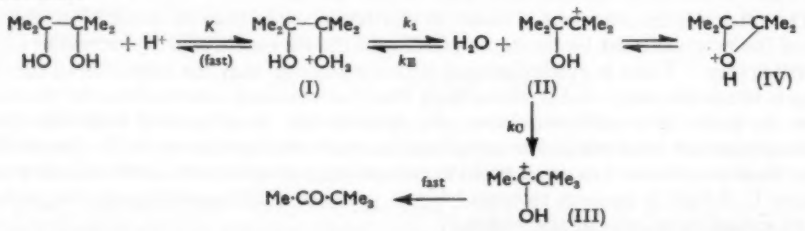
Discussion.—The nature of the acid catalysis of the rearrangement of pinacol is shown by comparisons of the rate in deuterium oxide and water,[4] and the molecularity is given by the plots of log k against $-H_0$ being straight lines of near unit slope (Table 1). The

TABLE 1. *Rate of rearrangement of pinacol in aqueous sulphuric acid at 72·9° and at 100°.*

At 72·9°							
$[H_2SO_4]$ (m)	0·055	0·108	1·33	1·85	2·46	2·83	3·37
10^4k (sec.$^{-1}$)	0·0086	0·016	0·386	0·737	1·26	1·67	2·80
$-H_0$	—	—	0·42	0·67	0·98	1·15	1·37
At 100°							
$[H_2SO_4]$ (m)	0·437	0·920	1·50	2·43			
10^4k (sec.$^{-1}$)	3·30	6·98	13·2	29·2			

At both temperatures the slope of log k against $-H_0 = 0{\cdot}90$. The rates calc. for 1·5m-H_2SO_4 fit the equation $k = 10^{19{\cdot}7} \exp(-33{,}700/RT)$ (sec.$^{-1}$).

unchanged pinacol, isolated after partial reaction, has partially exchanged its oxygen atoms with the solvent water. This exchange is acid-catalysed, and its rate-dependence upon acid concentration is similar to, but not identical with, that of rearrangement. We conclude that both exchange and rearrangement go through a common carbonium-ion intermediate.



The amount of oxygen exchange between the unchanged pinacol and water measures the extent to which the carbonium ion (II) is captured by the water molecules to regenerate

* Olefins are formed under certain conditions.[7a]

[6] Zucker and Hammett, *J. Amer. Chem. Soc.*, 1939, **61**, 2791.
[7] Duncan and Lynn, *J.*, 1956, 3512.
[7a] Fieser, "Experiments in Organic Chemistry," Heath, New York, 1941, 100.

pinacol. The amount of rearrangement measures the extent to which the carbonium ion (II) rearranges to give (III), which then decomposes rapidly to give pinacone. (We mention later why we believe that the last stage would be fast.) The rate of capture of the carbonium ions (II) by water will probably depend upon some function of the concentration, or perhaps the activity of water. The tendency for water to capture this carbonium ion will, therefore, decrease with increasing acidity (and decreasing water content) of the solution. On the other hand, the rate of rearrangement of the carbonium ion (II) ⟶ (III) should not depend much upon the water content of the solvent. The simplest series of reactions for this conversion is that shown; the methyl group migrates intramolecularly, (II) ⟶ (III), and the hydrogen attached to the oxygen atom is lost very rapidly as a proton, so playing no particular kinetic part in this partitioning of the carbonium ion but making the conversion (II) ⟶ (III) irreversible.

The relative rate constants, k_E and k_O, of these reactions of the carbonium ion (II) are given by:

$$\frac{\text{Rate of exchange}}{\text{Rate of rearrangement}} = \frac{k_E}{k_O} \propto [H_2O] \cdot \frac{f_{H_2O} \cdot f_{R^+}}{f_{ROH_2^+}}$$

In formulating this equation we assume that the transition states for exchange and rearrangement will be akin to the conjugate acid (I) and the carbonium ion (II) respectively and denote their activity coefficients as $f_{ROH_2^+}$ and f_{R^+} respectively.

Various obvious simplifications can be made to this equation. If the whole activity-coefficient term is neglected we can predict a linear dependence of k_E/k_O on the stoicheiometric concentration of water. Alternatively, neglect of the term $f_{R^+}/f_{ROH_2^+}$ predicts dependence upon the activity of water. In fact the results fit reasonably well with either hypothesis. However, the overall changes in the ratio k_E/k_O (Table 2), and in the water content of the solvent, are comparatively small, so the experimental uncertainty is not

TABLE 2. *Oxygen exchange in aqueous sulphuric acid at* 72·9°.

$[H_2SO_4]$ (m)	Time (hr.)	N_∞ (atoms % excess)	N_t (atoms % excess)	Reaction (%)	k_E/k_O
0·053	89	0·784	0·202	20	2·7
1·60	2·5	0·665	0·234	30	2·4
2·12	2·0	0·659	0·273	36	2·4
2·12 *	2·0	0·651	0·249	33	2·4
5·35	0·3	0·660	0·257	57	1·2

* [Pinacone] initially present equivalent to *ca.* half [pinacol]. As solutions were made up by weight it is convenient to express $[H_2SO_4]$ in terms of molality.

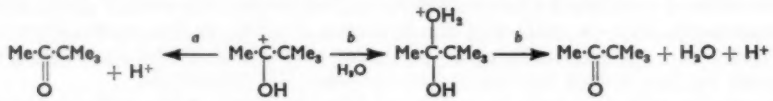
small by comparison with the changes in the ratio k_E/k_O. Further, as the solutions for the exchange experiments contained appreciable amounts of pinacol, we cannot attach any great significance to the exact numerical values of k_E/k_O for various acidities, although the direction of the changes is significant.

The rate of formation of pinacone is not the rate of formation of a carbonium ion from pinacol. It is in fact less than half this at low concentrations of acid. The complete rate equation for the formation of pinacone is: Rate $= Kk_1k_Oh_0[ROH]/(k_E + k_O)$, where [ROH] is the concentration of pinacol. This rate will be equal to that of formation of the carbonium ion $Kk_1h_0[ROH]$ only if $k_O \gg k_E$. This is obviously not so in the present experiments. However the ratio $k_O/(k_E + k_O)$ will not change much over a large change in acid concentration, and it will be sensibly constant relative to h_0. In going from 1·6m- to 5·35m-sulphuric acid, the ratio changes by *ca.* 2-fold, but h_0 changes *ca.* 30-fold. We can extrapolate this ratio to higher concentrations of acid, and calculate that in 50% sulphuric acid (w/w) more than 90% of the carbonium ions will rearrange to pinacone. Thus at higher acidities the rate of rearrangement will be the rate of formation of carbonium ions. Attempts were made to test this point, but unfortunately the rate of dissolution of the large amounts of pinacol required for the isotope experiments was slower than its rearrangements at these high acidities. Cases may exist where the partitioning

of the carbonium ion may change so rapidly with acidity that dependence of rate upon h_0 may be lost.

This general picture of the partitioning of the carbonium ion between solvent capture with oxygen exchange and a chemical reaction not requiring direct intervention of water, is very similar to that suggested for the acid-catalysed oxygen exchange and olefin elimination of *sec.*-butyl alcohol (Part II).

The formation of pinacone from the carbonium ion (III) could follow two routes, one a rapid loss of a proton (*a*), the other hydration followed by dehydration (*b*).



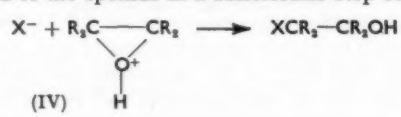
Oxygen exchange between water and ketones is much faster than the pinacol rearrangement, and so an experimental test between these two possibilities based upon isolation of pinacone from a rearrangement in $H_2{}^{18}O$ cannot be made,[8] although it might be feasible in other solvents.

We conclude from the exchange results that the conversion of the carbonium ion (II) into pinacone does not involve a water molecule in an activated step. The slow step must be the conversion of (II) into (III), possibly synchronised with proton removal, and if the ion (III) is attacked by water to form the hydrate of pinacone, this attack must be fast compared with the interconversion (II) ⟶ (III), and can have no kinetic significance on the overall rate of rearrangement or on this rate relative to that of oxygen exchange.

The rate of carbonium-ion formation is the sum of the rates of oxygen exchange and rearrangement, and can be compared with known rates of the unimolecular heterolysis of *tert.*-butyl alcohol in aqueous hydrochloric acid.[9] The rate of carbonium-ion formation from pinacol is *ca.* 1/50th of that of *tert.*-butyl alcohol (this assumes that the catalysing effects of hydrochloric and sulphuric acids are similar). There is therefore no assistance to bond fission from either the migrating methyl group or the hydroxyl oxygen atom. The decrease of rate has two probable causes: (1) the basicity of pinacol will be less than that of *tert.*-butyl alcohol, because of the increased size of the molecule and the $-I$ effect of the hydroxyl group; and (2) the rate of carbonium-ion formation from the conjugate acid will be decreased by this inductive effect of this hydroxyl group.

There are three alternative routes for oxygen exchange between water and unchanged pinacol other than *via* the formation and capture of a carbonium ion, but we now mention why we believe them to be unimportant.

(i) Oxygen exchange may go *via* the formation and hydrolysis of an epoxide but, as the acid hydrolysis of epoxides is unimolecular with formation of a carbonium ion from the conjugate acid of the epoxide (IV) as the slow stage,[10] such a route would be *via* a carbonium ion which is already involved in the rearrangement, and the rôle of the epoxide would merely be that of a species in equilibrium with the carbonium ion. It would be, for our experiments, equivalent to a temporary form of the carbonium ion, and this would not effect the interpretation of our results. A different situation might arise if the rates of rearrangement and oxygen exchange were compared in solutions containing appreciable amounts of halide ions, X^-. These are powerful nucleophilic reagents and they might attack the conjugate acid of the epoxide in a bimolecular step of the form:

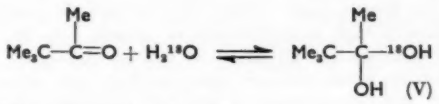


(IV)

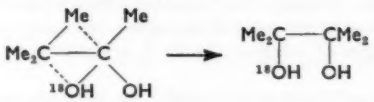
[8] Winstein and Ingraham, *J. Amer. Chem. Soc.*, 1955, **77**, 1738.
[9] Dostrovsky and Klein, *J.*, 1955, 791.
[10] Pritchard and Long, *J. Amer. Chem. Soc.*, 1956, **78**, 2667.

(ii) Oxygen exchange *via* bimolecular attack of a water molecule upon the conjugate acid of pinacol (I) is very unlikely. It would be an S_N2 attack by water upon a tertiary atom of a compound having a highly substituted β-carbon atom, and the steric compressions in such a bimolecular transition state would be very great. Further the kinetic form for the rate of oxygen exchange at various acid concentrations is powerful evidence against such a mechanism of exchange.

(iii) The exchange of oxygen atoms between ketones and water is rapid in acid solution [11] and so the oxygen atom of pinacone will be in isotopic equilibrium with the water *via* a reversible hydration:



If this hydrate (V) could rearrange to pinacol



the pinacol so formed would be isotopically enriched. Such a reaction seems unlikely, because the pinacol–pinacone rearrangement is irreversible and goes to completion. It was excluded explicitly by showing that the ratio of the rates of oxygen exchange and rearrangement was almost independent of added pinacone (Table 2). Added pinacone decreased the extents of both oxygen exchange and rearrangement to the same slight extent (*ca.* 10%). This could be because it, like other organic molecules,[12] decreases the acidity as measured by H_0, and because in the amounts added it formed a separate layer into which some of the pinacol might have been extracted.

Recently this problem of the pinacol rearrangement has been attacked by a study of kinetic isotope effects.[13] Pinacol was labelled with ^{14}C on either the " methyl " or the " alcoholic " carbon atoms. The ^{14}C-labelled pinacols rearranged less rapidly than the unlabelled compounds above 78°, with concentrations of the catalysing hydrochloric acid <0·2M. The isotope effects were very large, and much greater than those normally observed in bond-breaking processes. They suggest that both the breaking of the carbon–oxygen bond and the migration of the methyl group are activated processes, in agreement with evidence reported here and elsewhere. However, no kinetic isotope effect was observed in an experiment at 60° with 0·995M-hydrochloric acid. The reason for this striking difference is not obvious. The two sets of experiments differ in both temperature and the concentration of the catalysing hydrochloric acid. Formation of the epoxide from a carbonium ion, and its reversion to this ion, would decrease any kinetic isotope effect (by making the distribution of the tracer random); if this occurred at low but not high temperatures the results would be explicable. Another source of uncertainty is that the comparatively high (*ca.* 1M) concentration of the nucleophilic chloride ion might affect some detail of the reaction path.

Experimental

Materials.—Pinacol (B.D.H.) was recrystallised from water as the hexahydrate, m. p. 46°. Its purity was checked by periodate titration.

Kinetics.—All reactions were followed by periodate titration of unchanged pinacol. At various times sealed tubes, containing aliquot portions of the reaction mixture, were removed from a thermostat, cooled, and broken under an excess of sodium hydrogen carbonate. An

[11] Cohn and Urey, *J. Amer. Chem. Soc.*, 1938, **60**, 679.
[12] Long and Paul, *Chem. Rev.*, 1957, **57**, 1.
[13] Duncan and Lynn, *Austral. J. Chem.*, 1957, **10**, 7.

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excess of standardised periodate solution was added and the mixture left overnight at room temperature; the iodine liberated on addition of potassium iodide was estimated by titration against sodium arsenite. The reaction mixtures remained colourless under all the experimental conditions (cf. ref. 7).

The first-order rate coefficients were evaluated graphically. The constants presented agree reasonably well with those given elsewhere.[7]

Isotope Exchange.—Solutions of isotopically normal pinacol, in isotopically enriched water containing sulphuric acid, were heated in sealed ampoules. After a definite time of heating the amount of reaction was determined by periodate titration.

Where comparison was possible (at low acidity), the amount of reaction found was similar to that calculated from the kinetic data. This suggests that the reaction rate is not changed greatly by the comparatively high concentration of pinacol (*ca.* 1M) used for the exchange experiments (Found for reaction for 89 hr. with 0·053m-H_2SO_4 at 72·9°, reaction = 20%. Calc., 22·5%). This difference arises because water, formed from pinacol during the reaction, dilutes the sulphuric acid, and because pinacol probably decreases the acidity, as measured by H_0. Comparison between the found and calculated amounts of reaction could not be made for experiments at the higher acidities. For these the times required for solution of the pinacol, and warming of the reaction mixture, are not negligible compared with the total reaction time. For these reasons the amounts of reaction (Table 2) are calculated from direct measurements by periodate titration.

After a suitable time the solutions were cooled; the pinacone separated, and was removed. Crystals of pinacol hydrate separated when the aqueous portion was cooled to 0°. These were washed with a little ice-cold water and dissolved in warm water. The traces of acid in this solution were exactly neutralised with bartya, and the barium sulphate was spun off. Water was removed under reduced pressure until crystals of pinacol hydrate separated. These were dehydrated by azeotropic distillation with benzene at the pressure of a water pump. This reduced losses of pinacol by co-distillation with benzene. The dried pinacol was then distilled under reduced pressure and stored in a desiccator. A portion was pyrolysed to carbon monoxide *in vacuo* on red-hot carbon heated by a radio-frequency induction furnace. The carbon monoxide was analysed mass spectrometrically.

The usual scale of the experiments was 24 g. of pinacol hexahydrate (air dried) dissolved in 100 g. of acidified $H_2{}^{18}O$. In calculating the extent of isotopic exchange, allowance was made for the water of crystallisation of the pinacol.

In all experiments the concentration of pinacol was small relative to that of water, and the relative rates of oxygen exchange and chemical reaction are given by

$$k_E/k_O = [2\log N_\infty/(N_\infty - N_t)]/\{\log [a/(a - x)]\}$$

where a and $a - x$ are respectively the concentrations of pinacol initially and at the time of isolation, t, and N_∞ and N_t are respectively the isotopic abundance of pinacol calculated for complete exchange and found for the isolated material and measured in atoms % excess above normal.

The authors are indebted to Professors E. D. Hughes, F.R.S., and C. K. Ingold, F.R.S., and Mr. C. A. Vernon for helpful discussions, to Mr. P. Chaffe for assistance with the isotopic analysis, and to the Ministry of Education for a grant (to T. H.).

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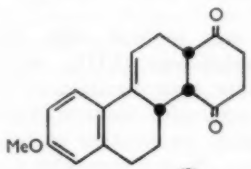
UNIVERSITY COLLEGE, LONDON, W.C.1. [*Received, September 12th*, 1957.]

74. *A New and Specific Aromatisation Reaction. Part III.* Aromatisation of Isolated* 1 : 4-*Dioxo*cyclo*hexane Rings.*

By P. A. Robins and James Walker.

The aromatisation of a 1 : 4-dioxo*cyclo*hexane ring to give an alkyl aryl ether in presence of chloroformic hydrogen chloride and an alcohol (Parts I and II) is now shown to occur, though only to a limited extent, in compounds in which this ring remains isolated from a centre of unsaturation. The olefinic double bond in the examples now described does not migrate into conjugation with the newly created aromatic ring. These observations are taken to illustrate the separate occurrence of the later phases of the mechanism already proposed (Part I).

In Part I* we described the ready and extensive conversion of *cis-syn*-1 : 2 : 3 : 4 : 5 : 6 : 12 : 13 : 14 : 15-decahydro-8-methoxy-1 : 4-dioxochrysene (I) into 1-alkoxy-5 : 6 : 11 : 12-tetrahydro-8-methoxychrysenes (II) by the action of chloroformic hydrogen chloride and an alcohol, and a mechanism was proposed in which the halo-



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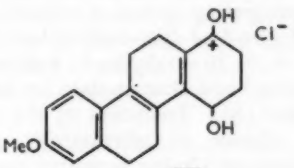

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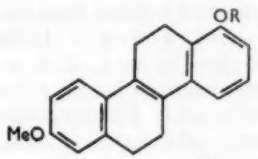

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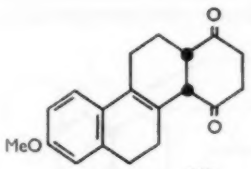

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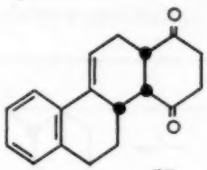

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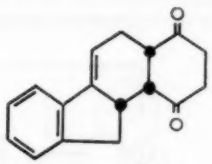

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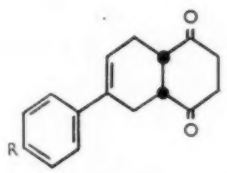

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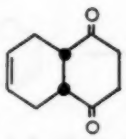

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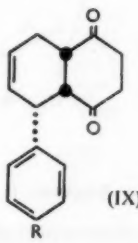


(IX)

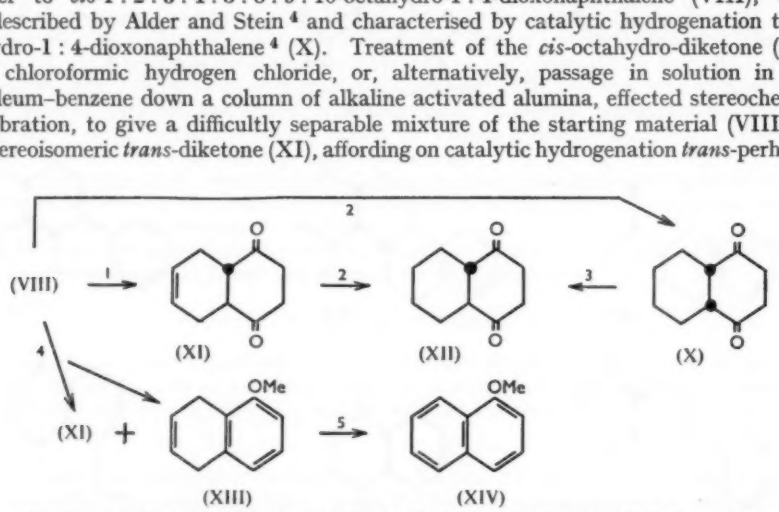
chromic salt (III), containing an extended conjugated system, was postulated as a precursor of the dialkoxytetrahydrochrysene (II). The latter (II; R = Et) was first obtained [1] as a by-product in the conversion of the diketone (I) into the isomeric $\Delta^{15:16}$-unsaturated ketone (IV) with hydrochloric acid in ethanol–chloroform, and this conversion was considered (Part I) to be the first stage in the conversion of the diketone (I) into the halochromic salt (III) and thence into the dialkoxytetrahydrochrysene (II). Similar aromatisations of the 1 : 4-dioxo*cyclo*hexane ring were demonstrated (Part II) in the

* Part I, *J.*, 1956, 3260; Part II, *J.*, 1957, 177.

[1] Robins and Walker, *J.*, 1956, 3249.

compounds (V), (VI), and (VII; R = H or MeO); each conversion took place in high yield, except that of the substance (VII; R = H), with which concomitant formation of a stereoisomeric diketone was observed. The low conversion in this one case was tentatively ascribed to inherent lack of mobility of the 6 : 7-double bond, rendering difficult the creation of the conjugated system necessary for halochromic salt formation. That the 6 : 7-double bond in the compound (VII; R = H) should be less labile than the corresponding double bond in the compound (VII; R = MeO) is in keeping with the lower mobility observed [2] for the 11 : 16-double bond in the dioxohydrochrysene (V) as compared with that in its methoxy-derivative (I). The present communication describes a further study of the exceptional compound (VII; R = H), together with a study of three new examples, *cis*-1 : 2 : 3 : 4 : 5 : 8 : 9 : 10-octahydro-1 : 4-dioxonaphthalene (VIII), *cis-syn*-1 : 2 : 3 : 4 : 5 : 8 : 9 : 10-octahydro-1 : 4-dioxo-5-phenylnaphthalene (IX; R = H), and *cis-syn*-1 : 2 : 3 : 4 : 5 : 8 : 9 : 10-octahydro-5-*p*-methoxyphenyl-1 : 4-dioxonaphthalene (IX; R = MeO), in which formation of extended conjugated systems and of halochromic salts of the type (III) are structurally impossible. Notwithstanding these structural limitations in the compounds (VIII) and (IX; R = H or MeO) aromatisation of the 1 : 4-dioxo*cyclo*hexane ring occurred in each case, but to a limited extent only, in presence of chloroformic hydrogen chloride and methanol, and the original olefinic double bond remained isolated from the participating centres of reaction.

cis-1 : 4 : 5 : 8 : 9 : 10-Hexahydro-1 : 4-dioxonaphthalene [3,4] was reduced with zinc powder to *cis*-1 : 2 : 3 : 4 : 5 : 8 : 9 : 10-octahydro-1 : 4-dioxonaphthalene (VIII), which was described by Alder and Stein [4] and characterised by catalytic hydrogenation to *cis*-perhydro-1 : 4-dioxonaphthalene [4] (X). Treatment of the *cis*-octahydro-diketone (VIII) with chloroformic hydrogen chloride, or, alternatively, passage in solution in light petroleum–benzene down a column of alkaline activated alumina, effected stereochemical equilibration, to give a difficultly separable mixture of the starting material (VIII) and the stereoisomeric *trans*-diketone (XI), affording on catalytic hydrogenation *trans*-perhydro-



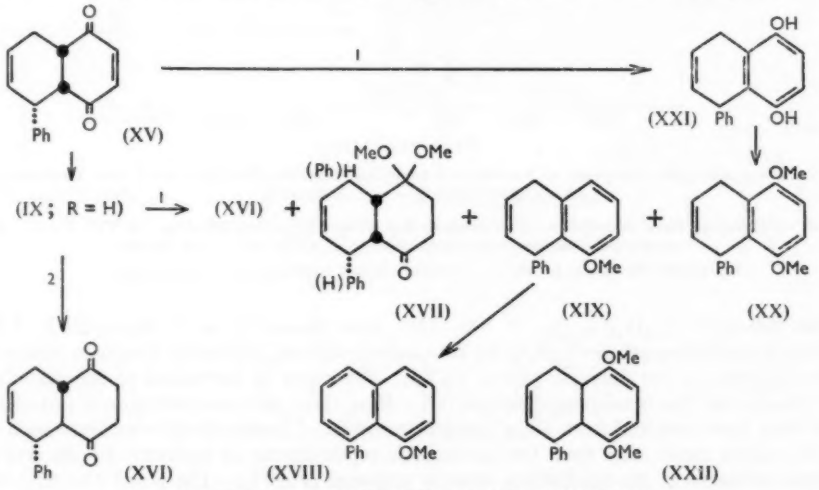
Reagents: 1, Al_2O_3 or HCl–$CHCl_3$; 2, H_2–Pd; 3, Ac_2O; 4, HCl–$CHCl_3$–MeOH; 5, −2H.

1 : 4-dioxonaphthalene (XII), identical with a specimen obtained by stereochemical equilibration of the *cis*-perhydro-diketone (X). When, however, methanol was added to the reaction mixture a third product was isolated in about 17% yield. This substance, an oil, had an ultraviolet light absorption spectrum of typical anisole type and gave, after purification through the picrate, analytical figures indicating the formula $C_{11}H_{12}O$. It was therefore 1 : 4-dihydro-5-methoxynaphthalene (XIII), in which the olefinic double bond has remained isolated from the aromatised ring, and dehydrogenation with chloranil afforded methyl α-naphthyl ether (XIV).

[2] Unpublished observation.
[3] Fieser, *J. Amer. Chem. Soc.*, 1948, **70**, 3165.
[4] Alder and Stein, *Annalen*, 1933, **501**, 247.

cis-syn-1 : 4 : 5 : 8 : 9 : 10-Hexahydro-1 : 4-dioxo-5-phenylnaphthalene [5] (XV) was reduced with zinc to give *cis-syn*-1 : 2 : 3 : 4 : 5 : 8 : 9 : 10-octahydro-1 : 4-dioxo-5-phenylnaphthalene (IX; R = H), whose ultraviolet light absorption spectrum indicated that the 6 : 7-double bond had not migrated into conjugation with the phenyl group; the stereochemical configuration is based on analogy.[6]

Stereochemical equilibration of the diketone (IX; R = H) by passage in solution through alkaline activated alumina gave initially a solid, m. p. 107—110°, which could be recrystallised without change in melting point from relatively concentrated solution and was at first considered to be a stereoisomeride of the diketone (IX; R = H). It was, however, subsequently found to be a mixture from which a pure stereoisomeric (?)*trans-anti*-1 : 2 : 3 : 4 : 5 : 8 : 9 : 10-octahydro-1 : 4-dioxo-5-phenylnaphthalene (XVI), m. p. 124—126°, could be obtained by seeding a dilute solution. The other component of the mixture could not be obtained pure. A similar mixture was obtained when the diketone (IX; R = H) was treated with hydrogen chloride in chloroform and then briefly with methanol. Treatment of the diketone (IX; R = H) with hydrogen chloride in chloroform and then with methanol at room temperature for 3 days gave a complex mixture. The crude product was roughly separated in the first instance into a solid (A) and an oil (B). Recrystallisation and hand-sorting resolved the solid (A) into the stereoisomeric diketone (XVI) already isolated from the stereochemical equilibration of the diketone (IX; R = H), and a substance $C_{16}H_{16}O(OMe)_2$, m. p. 123—124°, which was obviously a ketal (XVII) of the type previously encountered (Parts I and II). An attempt to determine its orientation was, however, unsuccessful. Chromatography of the oil (B) on alumina afforded four main fractions: (i) a substance $C_{17}H_{16}O$, m. p. 104—106°, containing one methoxyl group and having an ultraviolet light absorption spectrum indicative of an unconjugated anisole ring; (ii) a crystalline solid $C_{18}H_{18}O_2$, m. p. 108—110°, containing two methoxyl groups and having an ultraviolet light absorption spectrum indicative of a 1 : 4-dimethoxybenzene ring; (iii) the dimethyl ketal (XVII); and (iv) the *trans*-diketone (XVI).



The substance $C_{17}H_{16}O$, m. p. 104—106°, was dehydrogenated with chloranil to a compound $C_{17}H_{14}O$, m. p. 55—56°, which could have been either 1-methoxy-5- or -8-phenylnaphthalene (XVIII). An authentic specimen of 1-methoxy-5-phenylnaphthalene,

[5] Braude, Jones, and Stern, *J.*, 1947, 1087.
[6] Alder, Vagt, and Vogt, *Annalen*, 1949, **565**, 135.

XUM

prepared from 5-methoxy-1-tetralone and phenylmagnesium bromide, had m. p. 81—82°, and the difference between this compound and the substance $C_{17}H_{14}O$, m. p. 55—56°, was further demonstrated by differences in the fine structure bands observable in the ultraviolet light absorption spectra of the two substances, which, nevertheless, showed a gross overall similarity (Fig. 1) and were substantially different from the spectra of 1-methoxy-6- (Part II) and 1-methoxy-7-phenylnaphthalene (below). The substance $C_{17}H_{14}O$, m. p. 55—56°, must therefore have been 1-methoxy-8-phenylnaphthalene (XVIII), and its precursor $C_{17}H_{16}O$, m. p. 104—106°, must have been the dihydro-methoxy-phenylnaphthalene (XIX); unfortunately, attempts to synthesise 1-methoxy-8-phenylnaphthalene (XVIII) by a Gomberg or Bamberger free-radical coupling reaction, employing derivatives of 1-amino-8-methoxynaphthalene, gave only intractable tars. The free phenol, obtained on demethylation of the ether (XVIII) with hydrogen iodide in acetic anhydride, could not be obtained crystalline; it gave a strong blue colour with Gibbs's reagent [7] and was cryptophenolic.

FIG. 1. FIG. 2.

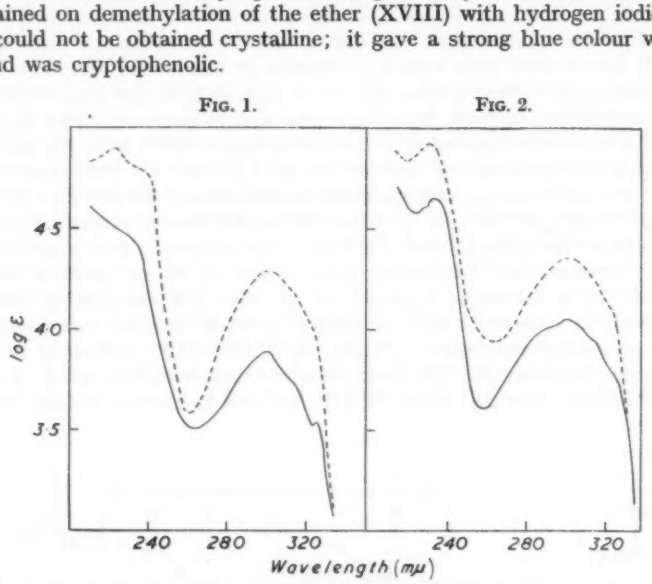


FIG. 1. *Ultraviolet light absorption of* 1-*methoxy*-8-*phenylnaphthalene* (XVIII) (——) *and* 1-*methoxy*-5-*phenylnaphthalene* (– – – –) *in hexane.*

FIG. 2. *Ultraviolet light absorption of* 1-*methoxy*-8-p-*methoxyphenylnaphthalene* (XXV) (——) *and* 1-*methoxy*-5-p-*methoxyphenylnaphthalene* (XXVI) (– – – –) *in hexane.*

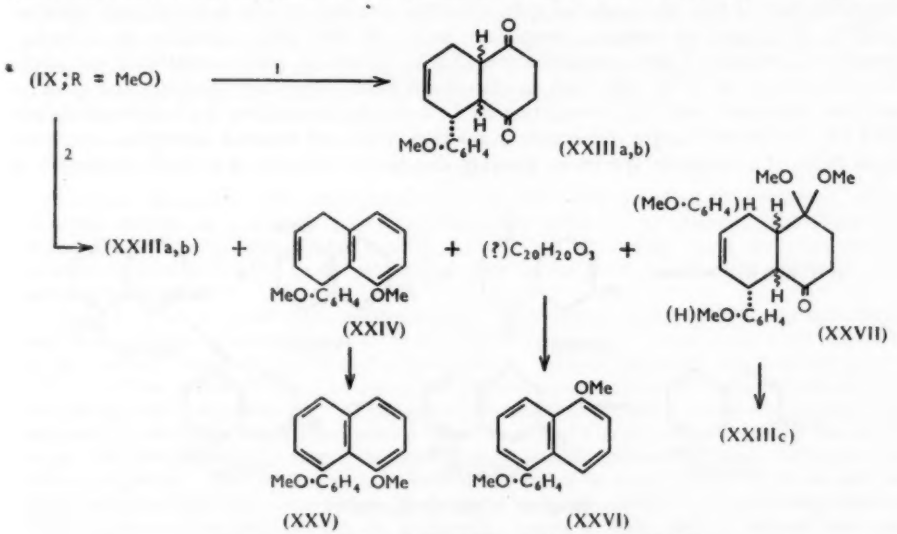
For clarity the curves for the 1 : 5-*derivatives are displaced by* + 0·3 in log ε.

The substance $C_{18}H_{18}O_2$, m. p. 108—110°, was shown to be 1 : 4-dihydro-5 : 8-dimethoxy-1-phenylnaphthalene (XX) by comparison with an authentic specimen obtained by methylation of the dihydric phenol (XXI); the mode of formation of the dimethyl ether (XX) from the octahydro-diketone (IX; R = H) in the aromatisation is not clear, but it may have resulted from aerial dehydrogenation of a dihydro-intermediate such as (XXII), which could arise from two metathetic replacements of hydroxyl by alkoxyl of the type indicated in the mechanism already proposed (Part I). The possibility that the dimethyl ether (XX) had arisen from traces of unchanged hexahydro-diketone (XV) in the starting material (IX; R = H) was discounted by the fact that under the conditions of the aromatisation, allowing nearly six days for interaction, only a trace of non-phenolic material was formed from the compound (XV), and that gave no readily eluted fluorescent material on chromatography. It is also of interest that the substance, m. p. 170°, described

[7] Gibbs, *J. Biol. Chem.*, 1927, **72**, 649.

by Weizmann, Bergmann, and Haskelberg [8] as the hexahydro-diketone (XV) was, in all probability, the dihydric phenol (XXI), m. p. 168—169°, resulting from the vigorous conditions used by these authors for isolation (distillation at 240°/0·2 mm.), and that Braude, Jones, and Stern [5] have reported that this change can take place on storage and is facilitated by exposure to light.

cis-syn-1 : 4 : 5 : 8 : 9 : 10-Hexahydro-5-*p*-methoxyphenyl-1 : 4-dioxonaphthalene [5] was reduced in the usual way to give *cis-syn*-1 : 2 : 3 : 4 : 5 : 8 : 9 : 10-octahydro-5-*p*-methoxyphenyl-1 : 4-dioxonaphthalene (IX; R = MeO), and stereochemical equilibration gave a mixture of two new stereoisomeric diketones (XXIIIa), m. p. 164°, and (XXIIIb), m. p. 135—136°. Treatment of the diketone (IX; R = MeO) in chloroform with hydrogen chloride followed by methanol for 24 hr. at room temperature gave the stereoisomeric diketone (XXIIIb) on crystallisation of the crude product. Chromatography of the material recovered from the mother-liquors on alumina gave a readily eluted compound, m. p. 123—124°, which from its analysis and ultraviolet light absorption spectrum appeared to be the expected 1 : 4-dihydro-8-methoxy-1-*p*-methoxyphenylnaphthalene (XXIV); dehydrogenation with chloranil gave 1-methoxy-8-*p*-methoxyphenylnaphthalene (XXV), whose structure followed from similar considerations to those applicable in the case of the corresponding phenyl derivative (XVIII) (above). The dehydrogenation product (XXV) differed from an authentic synthetic specimen of 1-methoxy-5-*p*-methoxyphenylnaphthalene (XXVI) in melting point and in the fine structure bands of its ultraviolet light absorption spectrum, although a gross overall similarity between the two spectra was again apparent (Fig. 2). When the treatment of the diketone (IX; R = MeO) with chloroformic hydrogen chloride and methanol was extended to 3 days a somewhat different result was obtained. Direct crystallisation of the product gave the stereoisomeric diketone (XXIIIa), m. p. 164°, in place of that (XXIIIb) of m. p. 135—136°, together with some



Reagents: 1, Al_2O_3 or HCl–$CHCl_3$; 2, HCl–$CHCl_3$–MeOH.

of the aromatisation product, 1 : 4-dihydro-8-methoxy-1-*p*-methoxyphenylnaphthalene (XXIV). Chromatography on alumina of the material recovered from the mother-liquors gave (i) a further quantity of the aromatisation product (XXIV), (ii) a small quantity of a substance, m. p. 76—76·5°, apparently $C_{20}H_{20}O_3$, (iii) a trace of the stereoisomeric diketone

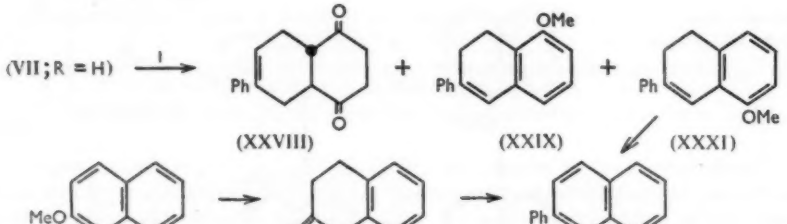
[8] Weizmann, Bergmann, and Haskelberg, *J.*, 1939, 391.

XUM

(XXIIIa), m. p. 164°, and (iv) a substance, m. p. 132—133°, which from its analysis and ultraviolet light absorption appeared to be a dimethyl ketal (XXVII) of the type previously encountered. Although the small amount of material available precluded an extensive study, the substance of m. p. 76—76·5° appeared to contain two methoxyl groups; its ultraviolet light absorption spectrum was very similar to that of the aromatisation product (XXIV) but dehydrogenation in the usual way with chloranil afforded 1-methoxy-5-*p*-methoxyphenylnaphthalene (XXVI). The ketal (XXVII), m. p. 132—133°, on hydrolysis with aqueous acetic acid, afforded a fourth stereoisomeric diketone (XXIIIc) of m. p. 155—156°. Apart from the starting material (IX; R = MeO) we are not in a position to assign configurations to these four stereoisomerides (IX; R = MeO) and (XXIII*a*, *b*, *c*).

The formation of an aromatised product in relatively low yield together with stereoisomeric diketone(s) in each of the three examples described above recalled the apparently anomalous behaviour of *cis*-1 : 2 : 3 : 4 : 5 : 8 : 9 : 10-octahydro-1 : 4-dioxo-6-phenylnaphthalene(VII; R = H) described in Part II, and this was therefore re-investigated.

It had been found previously in the treatment of the diketone (VII; R = H) overnight with chloroformic hydrogen chloride and then methanol that approximately 20% of crude aromatised product was obtained on chromatography of the material left after separation of the stereoisomeric *trans*-diketone (XXVIII), and on crystallisation of the crude aromatisation product to give 1 : 2-dihydro-8-methoxy-3-phenylnaphthalene (XXIX) a non-crystalline fluorescent oil remained in the mother-liquors. In order to obtain a further quantity of this oil the experiment was repeated on a larger scale and the reaction was allowed to proceed for nearly three days. Crystallisation of the crude product then afforded the aromatised product (XXIX) (*ca.* 16%). The non-crystalline material recovered from the mother-liquors was chromatographed on alumina, affording a readily eluted colourless fluorescent oil (28%), together with other more strongly adsorbed products. Repeated crystallisation of this oily material gave a further quantity of the aromatisation product (XXIX) (5%) and an isomeric compound, m. p. 59—60° (6%), affording on dehydrogenation 1-methoxy-7-phenylnaphthalene (XXX), identical with a synthetic specimen. The compound, m. p. 59—60°, had an ultraviolet light absorption spectrum and gave an analysis consistent with its formulation as 1 : 2-dihydro-5-methoxy-3-phenylnaphthalene (XXXI), but showed slight differences in melting point and infrared absorption spectrum from those of a synthetic specimen, possibly due to the presence of a small proportion of



Reagent: I, HCl–$CHCl_3$–MeOH.

the 1 : 4-dihydro-isomeride. Synthesis of 1-methoxy-7-phenylnaphthalene (XXX) was accomplished in a similar manner to that employed for the 6-phenyl isomer (Part II). Reduction of 1 : 7-dimethoxynaphthalene (XXXII) with sodium and alcohol, followed by acid hydrolysis, gave the previously unknown 8-methoxy-2-tetralone (XXXIII). Reaction with phenylmagnesium bromide and dehydration with formic acid then afforded 1 : 2-dihydro-5-methoxy-3-phenylnaphthalene (XXXI), which, as indicated above, showed

slight differences in properties from the product of the aromatisation reaction. Dehydrogenation of the dihydro-compound (XXXI) with chloranil in the usual way gave 1-methoxy-7-phenylnaphthalene (XXX).

The four examples (VIII), (IX; R = H or MeO), and (VII; R = H), in which aromatisation of the 1 : 4-dioxo*cyclo*hexane ring has occurred to a relatively minor extent only under the influence of chloroformic hydrogen chloride and methanol, stand in marked contrast with the examples (I), (IV), (V), (VI), and (VII; R = MeO) described in Parts I and II, in which aromatisation of the 1 : 4-dioxo*cyclo*hexane ring took place rapidly and in high yield. In the latter cases also the olefinic double bond migrated into conjugation with respect to both the pre-existent aryl group and the aromatic ring created in the reaction, in other words the products of the aromatisations described in Parts I and II were of substituted *trans*-stilbene type. The examples (VIII) and (IX) described in the present paper were chosen so as to obviate the fulfilment of similar structural conditions, and aromatisation of the 1 : 4-dioxo*cyclo*hexane ring has been shown to take place in these cases, although only in low yield, without concomitant migration of the olefinic double bond into a position in which it would ultimately be conjugated with the aromatic ring newly created. Furthermore, in the examples discussed in Parts I and II the aromatisation of the 1 : 4-dioxo*cyclo*hexane ring took place to give in high yield exclusively the product predicted by the mechanism outlined in Part I, whereas with at least two [(IX; R = MeO) and (VII; R = H)] of the examples described in the present paper the formation of alternative aromatisation products [(XXIV), (?)$C_{20}H_{20}O_3$, (XXIX), and (XXXI)] from the 1 : 4-dioxo*cyclo*hexane ring was observed; in one case (IX; R = H), the formation of the 1 : 4-dimethoxy-derivative (XX) was also noted.

These observations are taken to indicate that the ability to undergo the present aromatisation reaction is an inherent property of the 1 : 4-dioxo*cyclo*hexane ring, but the occurrence of aromatisation to the much greater extent observed in Parts I and II is attributable to the existence in the examples there discussed of halochromic salts of the type (III) as relatively more stable reaction intermediates than those concerned in aromatisations involving isolated 1 : 4-dioxo*cyclo*hexane rings.

Experimental

Routine ultraviolet light absorption measurements were made in 96% ethanol, unless otherwise stated, on a Unicam S.P. 500 Spectrophotometer. The existence and location of fine-structure features were kindly confirmed by Dr. G. H. Beaven using the photographic logarithmic cam method.[9] Light petroleum refers to the fraction of boiling range 60—80°, unless otherwise stated.

cis-1 : 2 : 3 : 4 : 5 : 8 : 9 : 10-*Octahydro*-1 : 4-*dioxonaphthalene* (VIII).—*p*-Benzoquinone (65 g.) and freshly distilled butadiene (40 g.) were allowed to react in glacial acetic acid (300 c.c.) in the manner described by Fieser.[3] The product, without isolation, was reduced by the addition of zinc powder (100 g.) in eight portions at intervals of several minutes with shaking and water-cooling as necessary. At the end of the reaction unused zinc and zinc acetate were removed by filtration and washed with a little benzene. The filtrate was poured into much water, and the product was recovered, washed with aqueous sodium hydrogen carbonate, and dried in benzene. The benzene solution was concentrated to small bulk and treated with an equal volume of light petroleum; *cis*-1 : 2 : 3 : 4 : 5 : 8 : 9 : 10-octahydro-1 : 4-dioxonaphthalene (VIII) separated in needles (44 g.), m. p. 98—99°, raised to 103—105° by several recrystallisations. Alder and Stein [4] record m. p. 108°.

Stereochemical Equilibration of cis-1 : 2 : 3 : 4 : 5 : 8 : 9 : 10-*Octahydro*-1 : 4-*dioxonaphthalene* (VIII). trans-1 : 2 : 3 : 4 : 5 : 8 : 9 : 10-*Octahydro*-1 : 4-*dioxonaphthalene* (XI).—A solution of the *cis*-compound (VIII) (2·0 g.) in alcohol-free chloroform (20 c.c.) was saturated with dry hydrogen chloride at 0° and kept at room temperature overnight. The clear, pale yellow solution was washed successively with water (twice), with aqueous sodium hydrogen carbonate,

[9] Holiday, *J. Sci. Instr.*, 1937, **14**, 166.

and finally with water, then filtered and evaporated under reduced pressure with gentle warming. (This working-up procedure was followed in all hydrogen chloride–chloroform treatments and is subsequently designated " in the usual way.") The pasty residue was extracted several times with boiling light petroleum, and the extracts were filtered from a small insoluble residue, clarified by the addition of a few drops of ethanol, and set aside. The fine needles that separated afforded, after several crystallisations from light petroleum, trans-1 : 2 : 3 : 4 : 5 : 8 : 9 : 10-*octahydro*-1 : 4-*dioxonaphthalene* (XI) as colourless plates (0·80 g.), m. p. 96—97° (Found: C, 73·2; H, 7·6. $C_{10}H_{12}O_2$ requires C, 73·2; H, 7·4%). The mother-liquors on concentration gave a small quantity of unchanged *cis*-stereoisomer (VIII), m. p. 102—103°.

Catalytic hydrogenation of the *trans*-octahydro-diketone (XI) (0·40 g.) in methanol (20 c.c.) in the presence of 2% palladised strontium carbonate (100 mg.) gave *trans*-perhydro-1 : 4-dioxonaphthalene (XII) (0·32 g.), which separated from light petroleum in leaflets, m. p. 119°. Alder and Stein [4] record m. p. 122° for the saturated *trans*-diketone (XII), prepared by the action of hot acetic anhydride on the saturated *cis*-diketone (X); repetition of this experiment gave a product identical in m. p. and mixed m. p. with our sample described above.

Action of Hydrogen Chloride and Methanol in Chloroform on cis-1 : 2 : 3 : 4 : 5 : 8 : 9 : 10-*Octahydro*-1 : 4-*dioxonaphthalene* (VIII). 1 : 4-*Dihydro*-5-*methoxynaphthalene* (XIII).—A solution of the *cis*-diketone (VIII) (10 g.) in alcohol-free chloroform (200 c.c.) was cooled in ice and saturated with dry hydrogen chloride. The initially non-fluorescent solution then showed a milky-white fluorescence in ultraviolet light. Methanol (10 c.c.) was added and the solution was kept at room temperature for 60 hr. before being worked up in the usual way. The resulting dark brown oil was extracted repeatedly with boiling light petroleum (b. p. 40—60°) until only a small tarry residue remained. The combined extracts on cooling deposited crystals together with a little brown gum. The crystals were of two forms which could be roughly separated by flotation. Repeated recrystallisation from light petroleum gave small quantities of the starting material (VIII) and its *trans*-stereoisomer (XI). The original light petroleum extracts, after separation of the crystalline material, showed a pale blue fluorescence in ultraviolet light, and were chromatographed on a column of alumina (150 g.; Peter Spence and Sons, Ltd., Type H). Elution with light petroleum (b. p. 40—60°) and light petroleum–benzene (9 : 1) afforded on evaporation a pale blue-fluorescing oil (1·69 g.), n_D^{22} 1·5682, part of which was distilled in a bulb tube, having b. p. 140° (bath temp.)/18 mm., n_D^{22} 1·5702, $\lambda_{max.}$ 270 mμ (log ε 3·25). The distilled material rapidly showed an increase in viscosity and became yellow, and satisfactory analytical figures were only obtained on a sample regenerated from the picrate and then distilled (Found: C, 82·2; H, 7·4; MeO, 19·8. $C_{11}H_{12}O$ requires C, 82·5; H, 7·6; 1MeO, 19·4%). The analysis and the ultraviolet light absorption showed the substance to be 1 : 4-*dihydro*-5-*methoxynaphthalene* (XIII). The crude product readily formed a rather unstable *picrate*, which separated from concentrated alcoholic solution in orange-red needles, m. p. 115—116° (Found: C, 52·1; H, 3·9; N, 10·8. $C_{11}H_{12}O,C_6H_3O_7N_3$ requires C, 52·5; H, 3·9; N, 10·8%).

Dehydrogenation of the dihydromethoxynaphthalene (XIII) (0·5 g.) in boiling propionic acid (20 c.c.) with chloranil (0·85 g., 1·1 equiv.) for 6 hr., followed by dilution with ether, washing with excess of alkaline sodium dithionite solution and evaporation of the ether afforded an oil, b. p. 140—143° (bath temp.)/19 mm., n_D^{22} 1·6214, having an infrared absorption spectrum identical with that of methyl α-naphthyl ether, and giving a picrate, m. p. 128—129°, identical with that of methyl α-naphthyl ether.

cis-syn-1 : 4 : 5 : 8 : 9 : 10-*Hexahydro*-1 : 4-*dioxo*-5-*phenylnaphthalene* (XV).—A mixture of 1-phenyl-1 : 3-butadiene [10] (24·35 g.) and methanol (250 c.c.) was stirred and treated with *p*-benzoquinone (19 g.), added in portions. After dissolution was complete the mixture was kept at room temperature for a few hours, diluted with water (25 c.c.), and set aside overnight, a crystalline mass separating. Filtration afforded *cis-syn*-1 : 4 : 5 : 8 : 9 : 10-hexahydro-1 : 4-dioxo-5-phenylnaphthalene (XV) (30·45 g.), sufficiently pure for further use. Crystallisation from light petroleum afforded pale yellow plates, m. p. 100—102° (Found: C, 80·3; H, 6·0. Calc. for $C_{16}H_{14}O_2$: C, 80·6; H, 5·9%). Braude, Jones, and Stern [5] record m. p. 101°.

cis-syn-1 : 2 : 3 : 4 : 5 : 8 : 9 : 10-*Octahydro*-1 : 4-*dioxo*-5-*phenylnaphthalene* (IX; R = H).—The above *cis*-hexahydro-diketone (XV) (30·4 g.) in glacial acetic acid (300 c.c.) was treated at room temperature with zinc powder (30 g.), added in portions with shaking and cooling under running water during 5 min. A further quantity (30 g.) of zinc powder was then added in one

[10] *Org. Synth.*, 1950, **30**, 75.

lot and shaking was continued for a further 5 min. After filtration and washing of the residue with benzene the filtrate was poured into water and extracted twice with benzene. The combined benzene layers were washed free from acetic acid, concentrated to small bulk under reduced pressure, and diluted with two volumes of light petroleum, affording cis-syn-1 : 2 : 3 : 4 : 5 : 8 : 9 : 10-*octahydro*-1 : 4-*dioxo*-5-*phenylnaphthalene* (IX; R = H) in the form of rods (26·7 g.), m. p. 139—140° (Found: C, 80·0; H, 6·8. $C_{16}H_{16}O_2$ requires C, 80·0; H, 6·7%). The ultraviolet light absorption spectrum showed a series of maxima in the region 255—265 mμ (log ε *ca.* 2·65), indicating that the remaining olefinic linkage was in the 6 : 7-position and not conjugated with the 5-phenyl group.

Stereochemical Equilibration of cis-syn-1 : 2 : 3 : 4 : 5 : 8 : 9 : 10-*Octahydro*-1 : 4-*dioxo*-5-*phenylnaphthalene* (IX; R = H).—(*a*) A solution of the *cis-syn*-diketone (IX; R = H) (2·0 g.) in alcohol-free chloroform (80 c.c.) was saturated with dry hydrogen chloride at 0°. After the addition of methanol (2 c.c.) the solution was kept at room temperature overnight and was then worked up in the usual way. Crystallisation of the solid residue from methanol afforded a *stereoisomer* (XVI) of (IX; R = H) in the form of stout needles, m. p. 124—126° (Found: C, 79·6; H, 6·9. $C_{16}H_{16}O_2$ requires C, 80·0; H, 6·7%), $\lambda_{max.}$ 260, 292 mμ (log ε 2·39 and 1·83 respectively). (*b*) Passage of a solution of the *cis*-diketone (IX; R = H) (1·0 g.) in benzene–light petroleum (b. p. 40—60°) (1 : 1) down a column of activated alumina (20 g.) gave, on further elution with benzene and evaporation of the eluate, a solid residue (1·0 g.), which after several crystallisations from methanol, again gave the diketone (XVI) (0·31 g.), m. p. 124—125°, stereoisomeric with (IX; R = H).

Action of Hydrogen Chloride and Methanol in Chloroform on cis-syn-1 : 2 : 3 : 4 : 5 : 8 : 9 : 10-*Octahydro*-1 : 4-*dioxo*-5-*phenylnaphthalene* (IX; R = H).—A solution of the *cis-syn*-diketone (IX; R = H) (10 g.) in alcohol-free chloroform (200 c.c.) was cooled in ice and saturated with dry hydrogen chloride. Methanol (10 c.c.) was added to the pale yellow solution, and the mixture was kept at room temperature for 65 hr. The then dark solution was worked up in the usual way and a solution of the residual oil in methanol (15 c.c.) was set aside to allow crystallisation to take place. The solid which separated was washed with methanol by decantation, and the combined mother-liquors and washings gave on concentration two further crops of solid. The three crops were combined (A). The final mother-liquor (B) was retained and examined as described below.

The solid (A), on further crystallisation from methanol, gave a mixture of needles and nodules, which were separated by hand. The needles, after several recrystallisations from methanol, afforded the diketone (XVI) (1·6 g.), m. p. 124—126°, stereoisomeric with (IX; R = H). The nodules, after several recrystallisations from methanol, gave a *dimethyl ketal* (XVII) as stout rods (0·82 g.), m. p. 123—124°, depressed to 100—105° on admixture with (XVI) (Found: C, 75·8; H, 7·8; MeO, 20·6. $C_{18}H_{22}O_3$ requires C, 75·5; H, 7·7; 2MeO, 21·7%), $\lambda_{max.}$ 261, 290 mμ (log ε 2·43 and 1·68 respectively). The infrared absorption spectrum showed a strong carbonyl-stretching band at 1710 cm.$^{-1}$.

The mother-liquors (B) were taken to dryness, giving a gum (6·32 g.) which was extracted repeatedly by dissolution in small volumes of benzene and addition of 9 volumes of light petroleum (b. p. 40—60°) until a small residue (0·22 g.) remained. The combined 9 : 1 petroleum–benzene extracts (500 c.c.) were allowed to percolate down a column of activated alumina (150 g.; Peter Spence and Sons, Ltd., Type H), and elution was continued with the same solvent mixture until a pale blue-fluorescing band (observed in ultraviolet light) had passed through. Evaporation of the eluate gave a fluorescent oil (1·64 g.), and crystallisation from methanol afforded 1 : 4-*dihydro*-8-*methoxy*-1-*phenylnaphthalene* (XIX) as needles (0·8 g.), m. p. 104—106° (Found: C, 86·6; H, 7·1; MeO, 12·5. $C_{17}H_{16}O$ requires C, 86·4; H, 6·8; 1MeO, 13·0%), $\lambda_{max.}$ 272, 279 mμ in hexane (log ε 3·32 and 3·31 respectively). Dehydrogenation of a sample in boiling anisole with chloranil (2·5 equiv.) for 18 hr., followed by dilution with benzene, washing with excess of alkaline sodium dithionite solution, and evaporation of the solvent, gave a dark oil. When the oil was treated with saturated alcoholic picric acid, a red picrate separated. This dissociated readily on recrystallisation, but a specimen was crystallised successfully from a small volume of methanol to give the *picrate* of 1-methoxy-8-phenylnaphthalene (XVIII) as red needles, m. p. 119° (Found: C, 59·9; H, 3·9; N, 8·9. $C_{17}H_{14}O,C_6H_3O_7N_3$ requires C, 59·6; H, 3·7; N, 9·1%). Regeneration from the picrate afforded a solid, m. p. 47—51°, which, on recrystallisation from methanol, gave 1-*methoxy*-8-*phenylnaphthalene* (XVIII) as tabular prisms, m. p. 55—56° (Found: C, 87·2; H, 6·1; MeO, 13·5. $C_{17}H_{14}O$ requires C, 87·1; H, 6·0;

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1MeO, 13·2%), $\lambda_{max.}$ 300, 326 mμ in hexane (log ε 3·89 and 3·54 respectively) (Fig. 1); fine structure bands were at 240, 287, 303, 308, 312, 315, 318, and 326 (vs) mμ.

Continued elution of the chromatogram with benzene–light petroleum (1 : 1) brought off a narrow bright blue-fluorescing band, and evaporation and crystallisation of the residue from methanol afforded 1 : 4-*dihydro*-5 : 8-*dimethoxy*-1-*phenylnaphthalene* (XX) as plates (0·35 g.), m. p. 108—110° (Found: C, 81·1; H, 7·0; MeO, 22·5. $C_{18}H_{18}O_2$ requires C, 81·2; H, 6·8; 2MeO, 23·3%), $\lambda_{max.}$ 288, 293 mμ (log ε 3·60 and 3·58 respectively).

Elution with benzene and then with chloroform brought off the dimethyl ketal (XVII) (0·8 g.), followed by the diketone (XVI) (1·27 g.), stereoisomeric with the starting material. Strongly adsorbed material (*ca.* 1·4 g.) remained on the alumina as a brown band.

Action of Hydrogen Chloride and Methanol on cis-syn-1 : 4 : 5 : 8 : 9 : 10-*Hexahydro*-1 : 4-*dioxo*-5-*phenylnaphthalene* (XV), *and Preparation of* 1 : 4-*Dihydro*-5 : 8-*dimethoxy*-1-*phenylnaphthalene* (XX).—A solution of the *cis-syn*-hexahydro-diketone (1·0 g.) in alcohol-free chloroform (40 c.c.) was saturated with dry hydrogen chloride at 0°. After the addition of methanol (5 c.c.) the solution was kept at room temperature for 6 days. The solution was then washed successively with water (twice), 2N-sodium hydroxide containing a little sodium dithionite, and water, and evaporated to a tar (0·14 g.). Chromatography of this residue on alumina showed that only strongly adsorbed material was present, and no evidence of a readily eluted fluorescent product was obtained.

Acidification of the alkaline washings with dilute hydrochloric acid gave a buff precipitate, which was collected, washed with water, and dried. Crystallisation from benzene afforded 1 : 4-*dihydro*-5 : 8-*dihydroxy*-1-*phenylnaphthalene* (XXI) as needles (0·5 g.), m. p. 168—169° (Found: C, 80·7; H, 6·4. $C_{16}H_{14}O_2$ requires C, 80·6; H, 5·9%). Methylation with dimethyl sulphate and alkali in methanol solution gave a brown powdery solid, which, on recrystallisation from methanol, afforded the ether (XX), m. p. 110—111°, identical with that obtained above.

1-*Methoxy*-5-*phenylnaphthalene* (cf. Baddar and El-Assal [11]).—5-Methoxy-1-tetralone [12] (3 g.) in ether (50 c.c.) was added to a boiling solution of phenylmagnesium bromide (from 0·8 g. of magnesium and 5·3 g. of bromobenzene) in ether (25 c.c.). After being heated under reflux for ½ hr., the mixture was cooled and decomposed with ice and dilute sulphuric acid. Evaporation of the ethereal solution gave an oil (4·32 g.) which was taken up in light petroleum (b. p. 40—60°) and allowed to percolate down a column of alumina (60 g.). Elution with the same solvent afforded a colourless oil (2·11 g.), which was freed from traces of diphenyl by steam-distillation. The resulting 1 : 2-dihydro-8-methoxy-4-phenylnaphthalene failed to crystallise, although Baddar and El-Assal [11] report m. p. 47—48°. Part (0·5 g.) of the product was dehydrogenated by heating it with chloranil (1·25 g., 2 equiv.) for 18 hr. in boiling anisole (25 c.c.). Working up as described above afforded 1-methoxy-5-phenylnaphthalene as leaflets, m. p. 81—82°; Baddar and El-Assal [11] report m. p. 84—85°. Ultraviolet light absorption max. in hexane were at 222, 235 (infl.), 299, 322 (infl.) mμ (log ε 4·60, 4·49, 3·99, and 3·77 respectively) (Fig. 1); fine structure bands were at 236, 240, 251, 276, 287, 301 (very broad), 310 (broad), 316, and 324 (vs) mμ.

cis-syn-1 : 4 : 5 : 8 : 9 : 10-*Hexahydro*-5-p-*methoxyphenyl*-1 : 4-*dioxonaphthalene*.—1-*p*-Methoxyphenylbut-2-en-1-ol [5] (5 g.) was heated in benzene (50 c.c.) with a crystal of iodine under reflux with the conventional Dean and Stark apparatus in the presence of a little *N*-phenyl-β-naphthylamine as a polymerisation inhibitor. Evolution of water (0·4 c.c.) ceased after 2 hr. and the benzene solution was cooled and treated with *p*-benzoquinone (3·26 g.). After 65 hr. at room temperature the solution was evaporated to dryness under reduced pressure, and crystallisation of the residue from methanol afforded *cis-syn*-1 : 4 : 5 : 8 : 9 : 10-hexahydro-5-*p*-methoxyphenyl-1 : 4-dioxonaphthalene (4·39 g.), m. p. 97—100°, raised to 106° on recrystallisation from light petroleum (b. p. 80—100°). Braude, Jones, and Stern [5] record m. p. 103°.

cis-syn-1 : 2 : 3 : 4 : 5 : 8 : 9 : 10-*Octahydro*-5-p-*methoxyphenyl*-1 : 4-*dioxonaphthalene* (IX; R = MeO).—The *cis-syn*-hexahydro-diketone (6·4 g.) was reduced with zinc powder (2 × 6·4 g.) in glacial acetic acid in the manner described above for similar reductions. Crystallisation of the crude product from benzene–light petroleum afforded cis-syn-1 : 2 : 3 : 4 : 5 : 8 : 9 : 10-*octahydro*-5-p-*methoxyphenyl*-1 : 4-*dioxonaphthalene* (IX; R = MeO) as prisms (4·28 g.), m. p. 113—114° (Found: C, 75·4; H, 6·8. $C_{17}H_{18}O_3$ requires C, 75·5; H, 6·7%), $\lambda_{max.}$ 278 mμ (log ε 3·29).

[11] Baddar and El-Assal, *J.*, 1951, 1844.
[12] Locket and Short, *J.*, 1939, 787.

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Stereochemical Equilibration of cis-syn-1 : 2 : 3 : 4 : 5 : 8 : 9 : 10-*Octahydro*-5-p-*methoxyphenyl*-1 : 4-*dioxonaphthalene* (IX; R = MeO).—(*a*) A solution of the *cis-syn*-diketone (IX; R = MeO) (1·0 g.) in alcohol-free chloroform (40 c.c.) was saturated with dry hydrogen chloride at 0°. After 24 hr. at room temperature the product was isolated in the usual way. Several crystallisations from benzene afforded a *stereoisomeric diketone* (XXIIIa) as fine needles, m. p. 164° (Found: C, 75·8; H, 6·7. $C_{17}H_{18}O_3$ requires C, 75·5; H, 6·7%), $\lambda_{max.}$ 278 mμ (log ε 3·22). The mother-liquors afforded a third *stereoisomeric diketone* (XXIIIb) as needles, m. p. 135—136° (Found: C, 75·5; H, 6·7%), $\lambda_{max.}$ 278 mμ (log ε 3·23). (*b*) A similar mixture of the two stereoisomers (XXIIIa and b) was obtained when a solution of the *cis-syn*-diketone (IX; R = MeO) in benzene–light petroleum was passed down a column of alkaline activated alumina, followed by elution with benzene.

Action of Hydrogen Chloride and Methanol in Chloroform on cis-syn-1 : 2 : 3 : 4 : 5 : 8 : 9 : 10-*Octahydro*-5-p-*methoxyphenyl*-1 : 4-*dioxonaphthalene* (IX; R = MeO).—(a) *For* 24 *hr.* A solution of the *cis-syn*-diketone (1·0 g.) in alcohol-free chloroform (40 c.c.) was saturated with dry hydrogen chloride at 0°, and methanol (2 c.c.) was then added. After 24 hr. the solution was worked up in the usual way. Several recrystallisations of the product from benzene–light petroleum gave the stereoisomeric diketone (XXIIIb) (0·52 g.), m. p. 135—136°, identical with that obtained as above. Chromatography of the material recovered from the mother-liquors, in benzene–light petroleum (b. p. 40—60°) (1 : 1) solution on a column of alumina (20 g.), gave a readily eluted fraction, crystallising from methanol to give 1 : 4-*dihydro*-8-*methoxy*-1-p-*methoxyphenylnaphthalene* (XXIV) as needles (70 mg.), m. p. 123—124° (Found: C, 81·1; H, 6·5; MeO, 23·3. $C_{18}H_{18}O_2$ requires C, 81·2; H, 6·8; 2MeO, 23·3%), $\lambda_{max.}$ 275 (infl.), 279, 283 (infl.) mμ in hexane (log ε 3·51, 3·57, and 3·34 respectively). Further elution of the column gave a small quantity (100 mg.) of the high-melting stereoisomer (XXIIIa), m. p. 159—160°, identical with that obtained previously.

Dehydrogenation of 1 : 4-dihydro-8-methoxy-1-*p*-methoxyphenylnaphthalene (XXIV) (0·5 g.) in boiling anisole with chloranil (1·02 g.; 2·2 equiv.) for 21 hr., followed by the usual method of working-up, afforded a semi-solid tar. This was purified by percolation in benzene–light petroleum (1 : 1) down a column of alumina (15 g.). Elution with the same solvent (250 c.c.) and evaporation left a solid (0·38 g.), which, on crystallisation from methanol, afforded 1-*methoxy*-8-p-*methoxyphenylnaphthalene* (XXV) as laths, m. p. 77° (Found: C, 81·7; H, 5·9; MeO, 23·0. $C_{18}H_{16}O_2$ requires C, 81·8; H, 6·1; 2MeO, 23·5%), $\lambda_{max.}$ 234, 301, 325 mμ in hexane (log ε 4·65, 4·05 and 3·76 respectively) (Fig. 2); fine structure bands were at 288, 301, 306, 314, 322, and 326 mμ. The free phenol, obtained in a qualitative demethylation experiment by using hydrogen iodide and acetic anhydride, gave a deep blue colour with Gibbs's reagent.[7]

(b) *For* 72 *hr.* A solution of the *cis-syn*-diketone (IX; R = MeO) (10 g.) in alcohol-free chloroform (200 c.c.) was saturated with hydrogen chloride at 0°, then treated with methanol (10 c.c.) and set aside for 72 hr. at room temperature. Working up in the usual way gave a semi-solid residue, which was taken up in methanol–benzene and allowed to crystallise. The resulting solid (4·20 g.), after several crystallisations from benzene–light petroleum afforded the diketone (XXIIIa) (2·03 g.), m. p. 164°. The first mother-liquor from the recrystallisation of this substance gave, on concentration, clusters of stout prisms, which, after several further recrystallisations from benzene–light petroleum, afforded 1 : 4-dihydro-8-methoxy-1-*p*-methoxyphenylnaphthalene (XXIV) (0·78 g.), m. p. 123—124°, identical with that described in (a).

The original methanol–benzene mother-liquors were taken to dryness and the residue was extracted repeatedly with light petroleum (b. p. 40—60°)–benzene (9 : 1) until a small insoluble residue (0·7 g.) remained. The combined extracts (450 c.c.) were allowed to percolate down a column of alumina (150 g.), and elution with light petroleum–benzene (4 : 1) afforded a further quantity (0·31 g.) of 1 : 4-dihydro-8-methoxy-1-*p*-methoxyphenylnaphthalene (XXIV); the mother-liquors from this gave amorphous material and needles on storage, and, after hand-sorting, several recrystallisations of the latter from methanol gave a *substance* as needles, m. p. 76—76·5° (Found: C, 77·7, 77·9; H, 6·4, 6·7; MeO, 19·6, 22·2. $C_{20}H_{20}O_3$ requires C, 77·9; H, 6·5; 2MeO, 20·1%), $\lambda_{max.}$ 275 (infl.), 280, 285 (infl.) (log ε 3·58, 3·64, and 3·44 respectively). Dehydrogenation of this substance (29 mg.) with chloranil (100 mg.) in anisole in the usual way afforded 1-methoxy-5-*p*-methoxyphenylnaphthalene (XXVI), identical (m. p., mixed m. p., and infrared absorption spectrum) with an authentic specimen (below).

Further elution of the column with benzene afforded a mixture, which was resolved into two

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components by crystallisation from benzene–light petroleum and hand-sorting. The minor component, m. p. 161—163°, was the high-melting stereoisomeric diketone (XXIIIa); the other component crystallised from benzene–light petroleum in prisms (1·0 g.) and was a *dimethyl ketal* (XXVII), m. p. 132—133° (Found: C, 72·5; H, 7·7; MeO, 29·4. $C_{19}H_{24}O_4$ requires C, 72·1; H, 7·6; 3MeO, 29·4%).

The ketal (XXVII) (0·12 g.) was dissolved in a few drops of warm acetic acid, and the solution was diluted with water and set aside to allow crystallisation to occur. The solid product was collected and crystallisation from benzene–light petroleum afforded a fourth stereoisomeric 1 : 2 : 3 : 4 : 5 : 8 : 9 : 10-*octahydro*-5-p-*methoxyphenyl*-1 : 4-*dioxonaphthalene* (XXIIIc) in the form of needles, m. p. 155—156°, depressed to below 135° on admixture with the stereoisomer (XXIIIa) of m. p. 164° (Found: C, 75·5; H, 6·6. $C_{17}H_{18}O_3$ requires C, 75·5; H, 6·7%) and with ultraviolet light absorption max. at 277, 285 mμ (log ε 3·27 and 3·17 respectively).

1-*Methoxy*-5-p-*methoxyphenylnaphthalene* (XXVI).—5-Methoxy-1-tetralone [12] (3·0 g.) in ether (30 c.c.) was added dropwise to a boiling solution of *p*-methoxyphenylmagnesium bromide (from 0·83 g. of magnesium and 6·4 g. of *p*-bromoanisole) in ether (30 c.c.). After 1 hr. under reflux the mixture was cooled and decomposed with ice and dilute sulphuric acid. The organic layer was separated, washed with dilute sulphuric acid and then with water, dried, and evaporated. The residue was distilled in steam for 1½ hr., the distillate being rejected, and again recovered as a crystalline solid. Recrystallisation from methanol–benzene afforded 1 : 2-*dihydro*-8-*methoxy*-4-p-*methoxyphenylnaphthalene* as laths (1·95 g.), m. p. 125—126° (Found: C, 81·2; H, 7·1; MeO, 22·7. $C_{18}H_{18}O_2$ requires C, 81·2; H, 6·8; 2MeO, 23·3%), $\lambda_{max.}$ 222, 273 mμ (log ε 4·57 and 4·02 respectively).

The dihydro-compound (0·5 g.) was dehydrogenated with chloranil (0·51 g.; 1·1 equiv.) in boiling anisole (25 c.c.) for 6 hr., and the product was isolated in the usual manner. Crystallisation from benzene–light petroleum afforded 1-*methoxy*-5-p-*methoxyphenylnaphthalene* (XXVI) as plates (0·42 g.), m. p. 130—131° (Found: C, 82·0; H, 5·9; MeO, 23·6. $C_{18}H_{16}O_2$ requires C, 81·8; H, 6·1; 2MeO, 23·5%), $\lambda_{max.}$ 231, 301, 322 (infl.) mμ in hexane (log ε 4·62, 4·06, and 3·81 respectively) (Fig. 2); fine structure bands were at 284·5, 301·5, 311, 316·5, and 324 mμ.

Action of Hydrogen Chloride and Methanol in Chloroform on cis-1 : 2 : 3 : 4 : 5 : 8 : 9 : 10-*Octahydro*-1 : 4-*dioxo*-6-*phenylnaphthalene* (VII; R = H).—A solution of the *cis*-diketone (VII; R = H) (9·0 g.) in alcohol-free chloroform (150 c.c.) was cooled in ice, saturated with dry hydrogen chloride, treated with methanol (9 c.c., *ca.* 10 equiv.), and then kept at room temperature for 64 hr. The mixture was worked up in the usual way, and crystallisation of the crude oily product from methanol–benzene gave 1 : 2-dihydro-8-methoxy-3-phenylnaphthalene (XXIX) (1·46 g.), m. p. 81—83°, identical with that previously isolated (Part II). The material recovered from the mother-liquor was extracted several times, with benzene–light petroleum (b. p. 40—60°) (1 : 9), the final tarry residue (2·0 g.) being rejected. The combined extracts were allowed to percolate down a column of alumina (80 g.) which was eluted with the same solvent mixture. Evaporation of the eluate (1 l.) gave a colourless oil (2·48 g.), showing a strong blue fluorescence in sunlight or ultraviolet light. The column was not further investigated.

Crystallisation of the fluorescent oil from methanol–benzene afforded a further quantity (0·83 g.) of 1 : 2-dihydro-8-methoxy-3-phenylnaphthalene (XXIX). The material from the mother-liquor was dissolved in a little light petroleum; when the solution was stored at 2° for 24 hr., nodules (1·11 g.) separated (m. p. 45—65°). Repeated crystallisation of the solid from light petroleum (b. p. 40—60°), combined with hand-sorting when practicable, afforded a still further quantity (0·26 g.) of the dihydro-compound (XXIX) and another component (XXXI), which crystallised from light petroleum (b. p. 40—60°) in nodular prisms (0·58 g.), m. p. 59—60° (Found: C, 86·6, 86·7; H, 6·8, 6·9; MeO, 12·6. $C_{17}H_{16}O$ requires C, 86·4; H, 6·8; 1MeO, 13·0%), $\lambda_{max.}$ 240, 312—322 (flat plateau) mμ in hexane (log ε 4·19 and 4·21 respectively). The infrared absorption spectrum in CCl_4 resembled in general, but showed significant variation from, that of authentic 1 : 2-dihydro-5-methoxy-3-phenylnaphthalene (XXXI), prepared as described below.

Dehydrogenation of this material, m. p. 59—60° (0·11 g.), with chloranil (0·23 g.; 2 equiv.) in boiling anisole for 16 hr. and isolation of the product in the usual way afforded, on crystallisation from methanol–benzene, 1-methoxy-7-phenylnaphthalene (XXX) as prisms (70 mg.), m. p. 67—68°, identical with an authentic specimen prepared as described below.

1 : 7-*Dimethoxynaphthalene* (XXXII).—Technical 1 : 7-dihydroxynaphthalene (50 g.), dissolved in water (220 c.c.) containing sodium hydroxide (29 g.), was methylated at *ca.* 70°

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under nitrogen by the dropwise addition of dimethyl sulphate (63 g.) with vigorous stirring. After dilution with water and extraction with ether, the ether layer was washed with water, 2N-sodium hydroxide, and water, then dried and fractionated to give 1 : 7-*dimethoxynaphthalene* (17·6 g.), b. p. 123—130°/0·4 mm., n_D^{22} 1·6208 (Found: C, 77·0; H, 6·5. $C_{12}H_{12}O_2$ requires C, 76·6; H, 6·4%).

8-*Methoxy*-2-*tetralone* (XXXIII).—1 : 7-Dimethoxynaphthalene (10·4 g.) was reduced in boiling butan-1-ol (250 c.c.) by the addition of sodium (20 g.) in pieces as rapidly as possible. When all the sodium had dissolved (1½ hr.), water (200 c.c.) and concentrated hydrochloric acid (200 c.c.) were added, and the mixture was heated on the steam-bath for ½ hr. with frequent shaking. The butanol was removed by steam-distillation and the crude product was recovered in ether, washed, and dried. The concentrated ethereal solution was shaken for 18 hr. with freshly prepared saturated sodium hydrogen sulphite solution (50 c.c.). The resulting bisulphite compound was collected, washed with ether, and decomposed in aqueous suspension with excess of sodium carbonate. Extraction with ether gave a solid (3·8 g.), and crystallisation from light petroleum (b. p. 40—60°) gave 8-*methoxy*-2-*tetralone* as needles, m. p. 58—59° (Found: C, 75·0; H, 7·1. $C_{11}H_{12}O_2$ requires C, 75·0; H, 6·9%).

1 : 2-*Dihydro*-5-*methoxy*-3-*phenylnaphthalene* (XXXI).—8-Methoxy-2-tetralone (1·5 g.) in ether (25 c.c.) was added to an ice-cold ether solution of phenylmagnesium bromide (from 0·63 g. of magnesium and 4·0 g. of bromobenzene), and the mixture was then heated under reflux for ½ hr. After cooling and decomposition with ice and dilute sulphuric acid, the ether layer was separated, washed, dried, and evaporated. The residue was freed from traces of diphenyl by steam-distillation, and the product was again recovered in ether. The resulting yellow oil (1·63 g.) was heated under reflux for 45 min. with anhydrous formic acid (20 c.c.), and the mixture was diluted with water and extracted with ether. The residue from the washed ethereal solution was allowed to percolate in benzene–light petroleum (b. p. 40—60°) (1 : 9) through a column of activated alumina (30 g.) and the blue-fluorescing band was eluted with benzene–light petroleum (1 : 9). The solid (1·1 g.) left on evaporation of the eluate (400 c.c.) was crystallised from light petroleum, to give 1 : 2-*dihydro*-5-*methoxy*-3-*phenylnaphthalene* (XXXI) as prisms, m. p. 51—52° (Found: C, 86·3; H, 6·7; MeO, 13·3. $C_{17}H_{16}O$ requires C, 86·4; H, 6·8; MeO, 13·0%), $\lambda_{max.}$ 235, 317 (infl.), 324 mμ with a broad flattened area in the range 315—328 mμ (log ε 4·22, 4·37, and 4·38 respectively).

1-*Methoxy*-7-*phenylnaphthalene* (XXX).—1 : 2-Dihydro-5-methoxy-3-phenylnaphthalene (0·2 g.) was dehydrogenated with chloranil (0·5 g., 2 equiv.) in boiling anisole for 22 hr. The mixture was worked up in the usual way, and the solid residue, crystallised from benzene–methanol, afforded 1-*methoxy*-7-*phenylnaphthalene* as prisms (0·16 g.), m. p. 67—68°, identical with the substance described above (Found: C, 87·0; H, 6·3; MeO, 13·5. $C_{17}H_{14}O$ requires C, 87·1; H, 6·0; MeO, 13·2%). Its ultraviolet light absorption max. in hexane were at 254, 303 mμ (log ε 4·72 and 3·97 respectively). The identity of this substance with that obtained above was confirmed by comparison of the infrared absorption spectra of the two substances.

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75. *The Alkali-metal Zirconium Ennea-alkoxides*, $MZr_2(OR)_9$.

By W. G. Bartley and W. Wardlaw.

Reactions of zirconium tetra-alkoxides, $Zr(OR)_4$, where R = Et, Pr^n, Pr^i, Bu^n, and Bu^s, and the alkoxides M(OR), where M = Li, Na, K, Tl, $Ca_{1/2}$ and Et_4N, were studied. With the alkali metals a series of stable double alkoxides with the general formula $MZr_2(OR)_9$ were obtained, many of which sublimed or distilled unchanged under reduced pressure. They are soluble in typical organic solvents, and molecular weights were determined ebullioscopically in benzene and in their parent alcohols. Vapour pressures were determined in the pressure range 0·1—10·0 mm. The formation of the double ennea-alkoxides in solution was confirmed by titration of the single alkoxides. These new compounds appear to be examples of covalently bound alkali metals.

In recent researches on alkoxides of Group IV elements [1] it was noted that when alcoholic solutions of the alkoxides were titrated with alkali-metal alkoxides, with thymolphthalein as indicator, the reaction could be expressed by the equation $MOR + 2Zr(OR)_4 \longrightarrow MZr_2(OR)_9$. This was confirmed from analysis of the products. These new compounds, conveniently referred to as ennea-alkoxides (or 9-alkoxides), were obtained when M = Li, Na, K, Tl, $Ca_{1/2}$, Et_4N, and R = Et, Pr^n, Pr^i, Bu^n, Bu^s. The ease with which they hydrolysed decreased in the order MeO > EtO > Pr^iO; consequently the *iso*propoxides were the most suitable for study. They were also the most readily obtained because the parent substance $Zr(OPr^i)_4$,Pr^iOH can be prepared pure by crystallisation from *iso*propyl alcohol. The solvated double alkoxide $LiZr_2(OPr^i)_9$,Pr^iOH is made conveniently from the single alkoxides and undergoes alcohol interchange in benzene solution. As a preparative method, however, alcohol interchange has limitations. Starting with lithium zirconium *iso*propoxide we found that primary alcohols interchanged completely but the method failed with *tert.*-butyl and *tert.*-amyl alcohols. In the latter cases the reaction proceeded readily to the stage $LiZr_2(OPr^i)_4(OR)_5$ but not beyond. In attempting to isolate $CoZr_4(OPr^i)_{18}$ from cobaltous chloride and $NaZr_2(OPr^i)_9$ in *iso*propyl alcohol a fine purple solid was obtained with the composition $Na_2[CoCl_2(OPr^i)_2]$. This is a new type of complex salt involving a Group VIII metal with co-ordinated alkoxide groups.

The molecular weights of several ennea-alkoxides were determined in boiling benzene

Table 1.

Compound	Mol. wt.	Mol. complexity	Compound	Mol. wt.	Mol. complexity
$LiZr_2(OEt)_9$	1240	2·1	$NaZr_2(OEt)_9$	710	1·2
$LiZr_2(OPr^n)_9$	1230	1·7	$NaZr_2(OPr^n)_9$	815	1·1
$LiZr_2(OBu^n)_9$	1330	1·6	$NaZr_2(OBu^n)_9$	858	1·0
$LiZr_2(OPr^i)_9$	760	1·0	$NaZr_2(OPr^i)_9$	761	1·0
$LiZr_2(OBu^s)_9$	847	1·0	$KZr_2(OBu^n)_9$	890	1·0
$LiZr_2(OEt)_4(OBu^t)_5$	737	1·0	$KZr_2(OPr^i)_9$	760 *	1·0
$LiZr_2(OPr^i)_9$,Pr^iOH	763	1·0	$Et_4NZr_2(OPr^i)_9$	1270	1·5

* In *cyclo*hexane.

and the results are given in Table 1. These figures show that most of the double alkoxides have the monomeric formula $MZr_2(OR)_9$ in contrast to zirconium tetra-alkoxides which are associated. Alcohol interchange of the dimeric lithium zirconium enneaethoxide with *tert.*-butyl alcohol causes the molecular complexity to decrease until the monomeric $LiZr_2(OEt)_4(OBu^t)_5$ is produced. In Table 2 the results are given of the molecular-weight determinations of some double alkoxides in boiling alcohols. All the compounds investigated were monomeric with the exception of tetraethylammonium zirconium ennea*iso*propoxide.

[1] Bradley and Wardlaw, *J.*, 1951, 280.

The fact that the ennea-*n*-butoxides tended to reflux rather than sublime led to attempts to measure b. p.s in a conventional semimicro-vacuum distillation apparatus. This proved unsatisfactory and a special apparatus was designed which allowed b. p.s to be measured at various pressures under total reflux. Rigid standardisation was necessary to ensure accuracy (cf. Bradley *et al.*[2]). The results are given in the form of plots of log P against $1/T$, and straight lines of the familiar form $\log P = a - b/T$ are obtained. These results are summarised in Table 3, where $T_{5\cdot0}$, L_v, and $\Delta S_{5\cdot0}$ are respectively the b. p. under 5·0 mm. pressure, the molar heat of vaporisation, and the entropy of vaporisation at 5·0 mm. pressure. The agreement between the duplicate sets of figures for lithium zirconium ennea*iso*propoxide and for zirconium tetra*iso*propoxide shows that the results are comparable both among themselves and to a less extent with those of Bradley,

TABLE 2.

Compound	Mol. wt.	Mol. complexity	Compound	Mol. wt.	Mol. complexity
$LiZr_2(OEt)_9$	605	1·0	$NaZr_2(OPr^i)_9$	720	1·0
$LiZr_2(OPr^i)_9$	703	1·0	$Et_4NZr_2(OPr^i)_9$	540	0·65
$LiZr_2(OPr^i)_9$,Pr^iOH ...	763	1·0			

TABLE 3.

Compound	*a*	*b*	$T_{5\cdot0}$	L_v	$\Delta S_{5\cdot0}$	Compound	*a*	*b*	$T_{5\cdot0}$	L_v	$\Delta S_{5\cdot0}$
$LiZr_2(OPr^n)_9$	14·4	7500	249°	34·3	65·7	$NaZr_2(OBu^n)_9$	13·0	6830	269	31·2	57·6
$LiZr_2(OPr^i)_9$	9·1	4150	219	19·0	38·6	$KZr_2(OBu^n)_9$	11·4	6060	292	27·7	49·0
,,	9·1	4160	221	19·0	38·4	$Zr(OPr^i)_4$ ...	16·3	7390	202	33·8	71·2
$LiZr_2(OBu^n)_9$	13·4	7000	278	32·0	58·1	$Zr(OPr^i)_4$ * ...	15·2	6895	204	31·5	66·0
$LiZr_2(OBu^s)_9$	14·2	6910	238	31·6	61·8	$Zr(OBu^t)_4$ †	9·9	3330	89	15·2	42·0
$NaZr_2(OPr^i)_9$	9·9	4590	222	21·0	42·4						

* Ref. 3. † Ref. 2.

Mehrotra, Swanwick, and Wardlaw.[3] The volatility of the double alkoxides coupled with the general involatility of their products of hydrolysis was of practical importance when purifying the former. The stabilities of the ennea-alkoxides varied and were dependent both on the alkyl group and on the alkali metal concerned. Thus the ennea-*n*-butoxides of lithium, sodium, and potassium sublimed without change in the alkali metal : zirconium ratio; so also did the solvated lithium zirconium ennea*iso*propoxide and sodium zirconium ennea*iso*propoxide. With potassium zirconium ennea*iso*propoxide an initial ratio of 0·504 decreased to 0·485 on sublimation, whilst with lithium zirconium ennea-*sec.*-butoxide the Li : Zr ratio changed from 0·500 to 0·439 after one sublimation. On the other hand, the mixed ennea-alkoxide $LiZr_2(OEt)_4(OBu^t)_5$ sublimed unchanged even under the drastic conditions of 200°/7·0 mm.

Most alkali zirconium double alkoxides are like the single alkoxides of aluminium and of zirconium and unlike those of the alkali metals in being soft solids which are very soluble in non-polar solvents. They differ similarly in melting and volatilising without decomposition when heated *in vacuo*, except for the salt $[Et_4N][Zr_2(OPr^i)_9]$. This compound is also exceptional in its osmotic properties, for whilst the lithium and the sodium zirconium ennea*iso*propoxides are both monomeric in boiling benzene or *iso*propyl alcohol the tetraethylammonium salt is associated (mol. complexity 1·5) in the first and dissociated (mol. complexity 0·65) in the second solvent. Moreover, the entropy of vaporisation ($\Delta S_{5\cdot0}$) for lithium zirconium ennea*iso*propoxide is even lower than that of zirconium *tert.*-butoxide,[2] so the former cannot dissociate on evaporation; this reinforces the conclusion that $LiZr_2(OPr^i)_9$ is monomeric in the vapour phase. It is very probable, therefore, that the alkali zirconium alkoxides are covalent. Confirmation is provided by comparing the b. p.s at 15 mm. of $LiZr_2(OPr^i)_9$ (extrapolated from Table 3) and of the hydrocarbon

[2] Bradley, Mehrotra, and Wardlaw, *J.*, 1952, 4202.
[3] Bradley, Mehrotra, Swanwick, and Wardlaw, *J.*, 1953, 2025.

containing an equal number of carbon atoms, *n*-$C_{27}H_{56}$ (interpolated from Karrer [4]). These are 248° and 276°, and the fact that the lithium compound boils at the lower temperature suggests that the screening effect of the *iso*propoxide groups is sufficiently complete to cause it to behave as a highly-branched hydrocarbon. The same must apply to $NaZr_2(OPr^i)_9$ and explains the similarity of its b. p. to that of the lithium analogue. As covalent compounds, the alkali zirconium alkoxides may be compared with the alkali ion complexes, their alkyls, and neutral covalent complexes. They obviously have little in common with the first group, most of which are salt solvates, or with the second, which are all polymerised with only the lithium derivatives volatile. They are, however, related to the third group more closely and it is of interest to reconsider the evidence for the covalent nature of the latter. In fact, it has depended mainly on the solubilities, often only slight, of the neutral alkali-metal complexes in non-polar solvents. Additional evidence was sometimes provided by an m. p. or the non-existence of corresponding compounds derived from isomers of the parent compound, but in no case did volatility unaccompanied by decomposition occur. It follows that the covalent character of the alkali zirconium alkoxides has been established with considerably greater certainty, since not only do they have very high solubilities in non-polar solvents and invariably melt if the pressure is high enough to prevent sublimation, but they can be distilled *in vacuo* without charring.

The sodium zirconium enneaethoxide was very soluble in ethyl alcohol but addition of a trace of water converted it into a crystalline compound which was sparingly soluble even in hot alcohol and could be recrystallised from hot benzene or toluene. It was also formed by adding excess of sodium ethoxide to a solution of any hydrolysed zirconium ethoxide having an ethoxide : zirconium ratio within the range 2·0—3·9. A hydrolysed solution of zirconium *n*-propoxide gave a substance of very similar solubility and appearance when similarly treated, but hydrolysed zirconium *n*-butoxide or *iso*propoxide gave gums. Analysis showed the composition of the crystalline compounds to be $Na_2Zr_3O(OR)_{12}$ with R = Et or Pr^n. The composition of the ethoxide was unchanged by ten consecutive crystallisations from benzene and it appeared to be involatile. The methoxide was obtained as a microcrystalline powder by alcohol interchange of the ethoxide with methyl alcohol. It was practically insoluble in either boiling methyl alcohol or benzene and was reconverted into the ethoxide by alcohol interchange. These results throw further light on the discrepancies between the work of Meerwein and Bersin [5] and that of Bradley and Wardlaw [1] on the preparation and properties of zirconium ethoxide and the sodium zirconium ethoxide. Thus Meerwein and Bersin obtained compounds of the type $NaH[Zr(OR)_6]$, where R = Me or Et, from reactions of alcoholic solutions of zirconium tetrachloride with sodium alkoxides. These compounds were sparingly soluble in alcohol but were crystallised from hot xylene. By treating the sodium zirconium alkoxide with the requisite amount of alcoholic hydrogen chloride, Meerwein and Bersin claimed to have obtained zirconium tetramethoxide and tetraethoxide as compounds soluble in benzene and which neutralised one equivalent of sodium methoxide when titrated with thymolphthalein as indicator. When Bradley and Wardlaw repeated this work they obtained a crystalline sodium zirconium ethoxide which was also insoluble in alcohol and soluble in hot benzene or xylene but their analytical data did not support the formula $NaH[Zr(OEt)_6]$ but were close to that for a hydrolysed product $Na_4Zr_6(OEt)_{21}(OH)_7$. Moreover, they found that pure zirconium tetraethoxide, prepared by another method, neutralised only half an equivalent of sodium ethoxide and that it was sparingly soluble in benzene or ethyl alcohol. Titration of zirconium tetraethoxide with sodium ethoxide has now confirmed Bradley and Wardlaw's results. When excess of sodium ethoxide was added to the tetraethoxide a small quantity of crystals was formed but with the composition $Na_2Zr_3O(OEt)_{12}$ which is close to that of Bradley and Wardlaw's product. On the other hand, the product isolated from the

[4] Karrer, "Organic Chemistry," New York, 1935, p. 30.
[5] Meerwein and Bersin, *Annalen*, 1929, **476**, 113.

reaction in which zirconium tetraethoxide was just neutralised with sodium ethoxide was the sodium zirconium enneaethoxide which was quite soluble in alcohol. We must therefore conclude that the crystalline product obtained by Meerwein and Bersin was $Na_2Zr_3O(OEt)_{12}$ and not $NaH[Zr(OEt)_6]$ and that their zirconium tetraethoxide was a product of hydrolysis. This view is supported by Bradley and Wardlaw's observation that the reaction of zirconium tetrachloride with an alcohol is accompanied by a side-reaction which produces water and leads to formation of a hydrolysed zirconium alkoxide. Also, the properties of Meerwein and Bersin's zirconium " tetraethoxide " are consistent with those of a hydrolysis product. Thus their product was soluble in alcohol and benzene and was involatile whereas Bradley and Wardlaw found, and we have confirmed, that the tetraethoxide is very sparingly soluble and sublimes *in vacuo*, whilst hydrolysed products of zirconium ethoxide with ethoxide : zirconium ratios of 2·0—3·5 are highly soluble in cold alcohol.

Experimental

Apparatus.—Special precautions of the type already described [2] were taken to exclude moisture, and all-glass apparatus was used.

Materials.—The zirconium tetrachloride, zirconyl chloride hydrate, lithium, sodium, potassium, and calcium used were all of laboratory reagent grade.

Analysis.—Zirconium was determined gravimetrically as ZrO_2. Alkali metals were determined in the ammoniacal filtrate after removal of zirconium. The solution was evaporated to dryness with the aid of an infrared heater. For sodium or potassium the residue was transferred mechanically *via* glazed paper to a platinum dish to which were also added rinsings of the evaporating basin. The dried residue in the platinum dish was then gently heated to remove ammonium chloride and the final residue was dissolved in water and the chloride determined by Mohr's method. For lithium determinations the use of glazed paper was prevented by the deliquescent nature of the chloride, so the first residue was dissolved in water and thus transferred to the platinum dish. Calcium was determined after removal of zirconium by precipitation as the oxalate followed by titration with potassium permanganate.[6] Thallium was determined as iodide [6] after removal of zirconium. Methoxide, ethoxide, and *iso*propoxide were determined by Bradley, Halim, and Wardlaw's method.[7]

Preparation of Zirconium Alkoxides.—The tetra alkoxides were prepared either by alcohol interchange with the *iso*propoxide *iso*propanolate [2,3] or from the tetrachloride [1] or from pyridinium zirconium hexachloride.[8] In addition, it was found convenient to prepare zirconium *iso*propoxide by starting from zirconyl chloride. A solution of zirconyl chloride octahydrate (32 g.) in *iso*propyl alcohol (400 c.c.), benzene (80 c.c.), and hydrochloric acid (40 c.c., *d* 1·18) was azeotropically dehydrated, and the anhydrous solution was then treated with excess of ammonia. After separation of ammonium chloride the filtrate was evaporated to dryness under reduced pressure, and the residue recrystallised from *iso*propyl alcohol. The crystalline fraction (20 g. Found: Zr, 24·4; Pr^iO, 72·8%) was near in composition to the *iso*propoxide *iso*propanolate (Calc.: Zr, 23·5; Pr^iO, 76·2%), whilst the residue obtained from the mother liquor (9 g. Found: Zr, 38·8; Pr^iO, 48·9%; Pr^iO/Zr, 1·95) was substantially " zirconyl " *iso*propoxide. The crystalline fraction was further purified by distillation at 200°/0·5 mm. followed by three recrystallisations of the distillate from *iso*propyl alcohol. The final product (10 g.) was the *iso*propoxide *iso*propanolate [Found: Zr, 23·8; Pr^iO, 75·3. Calc. for $Zr_3(OPr^i)_8$, $2Pr^iOH$: Zr, 23·5; Pr^iO, 76·2%].

Sodium Zirconium Enneamethoxide.—Sublimed (360°/0·005 mm.) zirconium tetramethoxide (4·8 g.) was treated with a solution of sodium (0·255 g.) in methyl alcohol (50 c.c.). The solution was evaporated under reduced pressure, and the residue heated at 290°/0·02 gave a white sublimate [Found: Na, 5·04; Zr, 38·4. $NaZr_2(OMe)_9$ requires Na, 4·75; Zr, 37·6%]. Although this sublimate was not the pure *enneamethoxide* it is noteworthy that it was more volatile than zirconium tetramethoxide.

Lithium Zirconium Enneaethoxide.—To a solution of lithium (0·144 g.) in ethyl alcohol

[6] Scott and Furman, " Standard Methods of Chemical Analysis," New York, 1939, Vol. 1, pp. 211, 942.

[7] Bradley, Halim, and Wardlaw, *J.*, 1950, 3450.

[8] Bradley, Halim, Sadek, and Wardlaw, *J.*, 1952, 2032.

(65 c.c.) was added zirconium tetraethoxide (11 g.), and the solution boiled for ½ hr. Evaporation failed to induce crystallisation and the residue finally obtained was distilled (260°/0·2 mm.) and gave a glassy distillate (7 g.) (Found: Li, 1·30; Zr, 31·5; EtO, 65·4%; Li/Zr, 0·54). Recrystallisation from benzene gave a microcrystalline *product* [Found: Li, 1·43; Zr, 30·5; EtO, 68·3. $LiZr_2(OEt)_9$ requires Li, 1·17; Zr, 30·7; EtO, 68·2%].

Sodium Zirconium Enneaethoxide.—Zirconium tetraethoxide (22·6 g.) was treated with the requisite quantity of boiling alcoholic 0·517N-sodium ethoxide (80·5 c.c.). The cooled solution was filtered to remove a small quantity of crystals and the filtrate was evaporated to dryness and the residue distilled at 230°/0·1 mm. The soft crystalline sublimate (18·3 g.) melted in a sealed tube under nitrogen over a range of 165—305°. A sample was heated under nitrogen until a clear melt was obtained, and then allowed to cool slowly and crystallise. Then it was reheated until about two-thirds was molten whereupon the liquid was decanted off the crystals and both were allowed to cool. Analysis showed that both fractions were the *enneaethoxide* (Found, for lower-melting fraction: Na, 3·73; Zr, 29·9; EtO, 64·8. Found, for higher-melting fraction: Na, 3·85; Zr, 30·0; EtO, 64·6. $NaZr_2(OEt)_9$ requires Na, 3·76; Zr, 29·9; EtO, 66·4%). The product readily dissolved in ethyl alcohol or benzene but the solutions were very easily hydrolysed.

Calcium Zirconium Octadecaethoxide.—Zirconium tetraethoxide (30 g.) was dissolved in ethyl alcohol (150 c.c.), and the solution refluxed with calcium (1·11 g.) for 12 hr. The cooled solution gave a white crystalline product (30 g.) [Found: Ca, 3·15; Zr, 29·1; EtO, 66·2. $CaZr_4(OEt)_{18}$ requires Ca, 3·30; Zr, 30·0; EtO, 66·7%]. The *compound* could be crystallised from hot benzene and was distilled at 280° *in vacuo*.

Lithium Zirconium Ennea-n-*propoxide.*—(*a*) Lithium (0·371 g.) was dissolved in a solution of zirconium *n*-propoxide (35 g.) in *n*-propanol (120 c.c.). Crystallisation could not be induced so the solution was evaporated to dryness and the residue on distillation (226°/0·3 mm.) gave a glassy distillate (34 g.) [Found: Li, 0·94; Zr, 25·5. $LiZr_2(OPr)_9$ requires Li, 0·96; Zr, 25·3%]. (*b*) Lithium zirconium ennea*iso*propoxide (10 g.) was caused to react with *n*-propyl alcohol (20 c.c.) in benzene (50 c.c.) and the liberated *iso*propyl alcohol was removed by azeotropic distillation. The solution was then evaporated to dryness, and the residue distilled (250°/0·5 mm.) to give a glassy solid (Found: Li, 0·98; Zr, 25·7%). The *lithium zirconium ennea*-n-*propoxide* gave the following vapour pressures: 211°/0·41 mm.; 216°/0·55; 226°/0·90; 235°/2·0; 240°/3·0; 244°/4·0; 250°/5·0; 263°/9·3. The distillate was analysed (Found: Li, 0·98; Zr, 25·7%).

Lithium Zirconium Ennea-n-*butoxide.*—Zirconium *n*-butoxide (32 g.) in *n*-butyl alcohol (100 c.c.) was boiled with lithium (0·290 g.) until all was dissolved. After evaporation to dryness the residue was distilled (221—235°/0·3 mm.) giving a colourless glass [Found: Li, 0·82; Zr, 21·7. $LiZr_2(OBu)_9$ requires Li, 0·82; Zr, 21·5%]. The following vapour pressures were obtained: 230°/0·32 mm.; 237°/0·46; 240°/0·65; 246°/0·80; 250°/1·1; 256°/1·5; 262°/2·1; 268°/3·3; 274°/4·3. The distillate was analysed (Found: Li, 0·82; Zr, 21·8%).

Sodium Zirconium Ennea-n-*butoxide.*—(*a*) Sodium (1·08 g.) was dissolved in *n*-butyl alcohol (100 c.c.) containing zirconium tetrabutoxide (34 g.). After evaporation of the solution to dryness the residue was distilled (218—225°/0·37 mm.) giving a white partially crystalline *product* (31 g.) which was very soluble in *n*-butyl alcohol and in benzene [Found: Na, 2·85; Zr, 21·3. $NaZr_2(OBu)_9$ requires Na, 2·64; Zr, 21·1%].

(*b*) Sodium zirconium ennea*iso*propoxide (10 g.) was caused to react with *n*-butyl alcohol (20 c.c.) in benzene (100 c.c.) and the liberated *iso*propyl alcohol was removed by azeotropic distillation. The solution was evaporated to dryness, and the residue distilled (Found: Zr, 21·2%). The following vapour pressures were obtained: 220°/0·29 mm.; 229°/0·50; 232°/0·59; 238°/0·9; 256°/2·6; 263°/3·5; 242°/1·2; 248°/1·6; 252°/2·0. The distillate was analysed (Found: Na, 2·85; Zr, 21·3%).

Potassium Zirconium Ennea-n-*butoxide.*—Potassium (2·65 g.) was dissolved in a solution of zirconium tetrabutoxide (26 g.) in butyl alcohol (80 c.c.) under nitrogen and the solution was evaporated to dryness. Distillation of the residue gave a pale yellow distillate (24 g.) (Found: K, 7·60; Zr, 19·5%) to which more zirconium butoxide (9·6 g.) was added and the mixture was distilled *in vacuo* to give a colourless distillate [Found: K, 4·44; Zr, 20·8. $KZr_2(OBu)_9$ requires K, 4·45; Zr, 20·7%]. The following vapour pressures were determined: 238°/0·38 mm.; 242°/0·48; 250°/0·66; 252°/0·80; 256°/0·92; 258°/1·1; 262°/1·4. The distillate was analysed (Found: K, 4·44; Zr, 20·8%).

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Lithium Zirconium Enneaisopropoxide isoPropanolate.—(*a*) Zirconium *iso*propoxide *iso*propanolate (127 g.) was refluxed in *iso*propyl alcohol (500 c.c.) with lithium (1·53 g.) until all was dissolved. The residue obtained after evaporation of the solvent was distilled (193°/1·0 mm.) and crystallised from *iso*propyl alcohol (300 g.). The *compound* (120 g.) was very soluble in benzene, light petroleum, ether, or acetone and it melted at 206° [Found: Li, 0·90; Zr, 23·4; Pr^iO, 76·4; active H, 0·134. $LiZr_2(OPr^i)_9,Pr^iOH$ requires Li, 0·89; Zr, 23·35; Pr^iO, 75·6; active H, 0·129%]. The compound sublimed at 160°/0·2 mm. (Found: Li, 0·95; Zr, 24·7; Pr^iO, 75·8%).

(*b*) Lithium zirconium enneaethoxide (10 g.) was caused to react with *iso*propyl alcohol (200 c.c.) until no more ethyl alcohol was liberated. The ennea*iso*propoxide *iso*propanolate (9 g., m. p. 204—206°) was obtained after twice recrystallising it from *iso*propyl alcohol.

Lithium Zirconium Enneaisopropoxide.—The foregoing product (19·5 g.) was heated at 200° under nitrogen at 10 mm. pressure and the pressure was gradually reduced to 2 mm., causing effervescence and melting. When effervescence ceased the mobile liquid was distilled and gave a colourless distillate which set to a hard solid [Found: Li, 0·965; Zr, 25·4. $LiZr_2(OPr^i)_9$ requires Li, 0·96; Zr, 25·3%]. The following vapour pressures were obtained: (*a*) 207°/3·0 mm.; 210°/3·5; 214°/4·0; 220°/5·0; 224°/6·0; 228°/7·0; 235°/9·0. (*b*) 208°/2·8; 217°/4·1; 223°/5·7; 230°/7·2; 238°/9·8; 232°/7·5; 228°/5·9; 221°/5·1. The distillates were analysed [Found: Li, (*a*) 0·96, (*b*) 0·98; Zr, (*a*) 25·4, (*b*) 25·4%].

Sodium Zirconium Enneaisopropoxide.—Zirconium *iso*propoxide *iso*propanolate (104 g.) and sodium (3·04 g.) were dissolved in boiling *iso*propyl alcohol (400 c.c.) and the solution evaporated to dryness. The residue was distilled at 260°/1 mm. and gave a hard solid distillate (92 g., m. p. 168—180° sealed tube) [Found: Na, 3·05; Zr, 24·9. $NaZr_2(OPr^i)_9$ requires Na, 3·12; Zr, 24·7%]. A sample (1·853 g.) was sublimed, giving a residue (0·287 g.; Pr^iO, 44%) and a sublimate (1·543 g. Found: Na, 3·07; Zr, 24·9; Pr^iO, 73·1%). The following vapour pressures were obtained: 196°/1·5 mm.; 202°/2·0; 210°/3·0; 215°/4·0; 220°/4·6; 228°/6·0.

Potassium Zirconium Enneaisopropoxide.—Zirconium *iso*propoxide *iso*propanolate (19·76 g.) in benzene (30 c.c.) was titrated with *iso*propanolic potassium *iso*propoxide (136·1 c.c., 0·198N), thymolphthalein being used as indicator. The end-point corresponded to K/Zr = 0·528. After removal of solvent the residue was sublimed at 200°/0·2 mm. [Found: K, 5·20; Zr, 24·1; Pr^iO, 72·9. $KZr_2(OPr^i)_9$ requires K, 5·19; Zr, 24·2; Pr^iO, 70·6%]. The *compound* was resublimed without change in composition and it was very soluble in ether, *iso*propyl alcohol, benzene, carbon tetrachloride, or light petroleum and it could not be crystallised from any of these solvents.

Thallium Zirconium Enneaisopropoxide.—Thallium (7 g.) was caused to react with vapour from boiling ethyl alcohol (100 c.c.) in a stream of oxygen (cf. Sidgwick and Sutton [9]) and the alcoholic solution of thallous ethoxide was interchanged with *iso*propyl alcohol (300 c.c.) and the ethyl alcohol removed by fractional distillation. To the resulting solution, zirconium *iso*propoxide *iso*propanolate (24 g.) was added and the solution was then concentrated to about 50 c.c. and allowed to cool. Large plate-like crystals which were deposited were filtered off and dried at 20°/0·5 mm. [Found: Tl, 20·8; Zr, 19·9. $TlZr_2(OPr^i)_9$ requires Tl, 22·2; Zr, 19·9%]. The *compound* was sublimed at 220°/0·5 mm. and gave needle crystals which contained thallium and zirconium.

Tetraethylammonium Zirconium Enneaisopropoxide.—Tetraethylammonium iodide (100 g.) in water was added to a boiling aqueous solution (3 l.) of lead chloride (72 g.). Lead iodide was filtered off, the filtrate evaporated to dryness, and the residue extracted with alcohol (500 c.c.). The alcoholic extract was concentrated until the tetraethylammonium chloride crystallised. The latter was dried at 100°/0·1 mm., dissolved in *iso*propyl alcohol (65·5 c.c.), and then treated with the requisite amount of *iso*propanolic sodium *iso*propoxide (200 c.c., 0·090N). The filtered solution was standardised acidimetrically and the requisite amount (190 c.c.) was treated with a solution of zirconium *iso*propoxide *iso*propanolate (9·3 g.) in benzene (20 c.c.). Evaporation of solvent left a brown gum [Found: Zr, 20·0. $(Et_4N)Zr_2(OPr^i)_9$ requires Zr, 21·6%]. The *compound*, heated at 180°/0·1 mm., suddenly effervesced and the pressure rose to 10 mm. before reverting to 1·0 mm. A colourless liquid distilled over at 194°/1·0 mm. and was evidently zirconium tetra*iso*propoxide since it crystallised from *iso*propyl alcohol in characteristic fashion. Further evidence for the dissociation of the tetraethylammonium ennea*iso*propoxide was afforded by an alkaline condensate collected in the cold trap. In another preparation the

[9] Sidgwick and Sutton, *J.*, 1930, 1461.

tetraethylammonium compound tended to crystallise from solution on standing. The crystals were dried at 100°/0·5 mm. [Found: Zr, 21·5; Pr^iO, 60·2. $(Et_4N)Zr_2(OPr^i)_9$ requires Zr, 21·6; Pr^iO, 63·0%].

Lithium Zirconium Ennea-sec.-*butoxide*.—Lithium zirconium ennea*iso*propoxide *iso*propanolate (20 g.) was caused to react with *sec.*-butyl alcohol (40 c.c.) in benzene (100 c.c.) and the liberated *iso*propyl alcohol was removed by fractional distillation. The resulting solution was evaporated to dryness and the residue was distilled at 200—210°/0·2 mm., giving a colourless solid distillate [Found: Li, 0·75; Zr, 22·3. $LiZr_2(OBu^s)_9$ requires Li, 0·82; Zr, 21·5%]. The following vapour pressures were obtained: 217°/1·3 mm.; 224°/2·0; 230°/3·1; 233°/3·5; 236°/4·5; 238°/5·0; 241°/6·0; 248°/8·4. The distillate was analysed (Found: Li, 0·63; Zr, 22·4%).

Lithium Zirconium Tetraethoxide Penta-tert.-*butoxide*.—Lithium zirconium enneaethoxide (21·4 g.) was caused to react with *tert.*-butyl alcohol (34 c.c.) in benzene (300 c.c.) and the liberated alcohol removed by azeotropic fractional distillation. Evaporation of the solvent gave a solid (28·2 g.) [Found: Zr, 23·8; EtO, 24·5. $LiZr_2(OEt)_4(OBu^t)_5$ requires Zr, 24·8; EtO, 24·5%]. The *compound* was sublimed at 140°/0·2 mm. (Found: Zr, 24·7; EtO, 24·9%) and distilled at 168—173°/0·3—0·5 mm. (Found: Li, 0·95; Zr, 24·9; EtO, 24·7%). The compound was very soluble in benzene but was crystallised from *tert.*-butyl alcohol and the crystals of *solvate* were dried at 20°/0·2 mm. [Found: Zr, 23·3; EtO, 22·9. $LiZr_2(OEt)_4(OBu^t)_5$,Bu^tOH requires Zr, 22·5; EtO, 22·3%].

*Lithium Zirconium Tetraiso*propoxide *Penta*-tert.-*butoxide*.—Lithium zirconium ennea*iso*propoxide *iso*propanolate (20 g.) was caused to interchange with *tert.*-butyl alcohol in the foregoing manner and the solid *product* finally obtained was dried at 80°/0·5 mm. [Found: Zr, 22·6; Pr^iO, 29·8. $LiZr_2(OPr^i)_4(OBu^t)_5$ requires Zr, 23·1; Pr^iO, 29·9%].

*Lithium Zirconium Tetraiso*propoxide *Penta*-tert.-*amyloxide*.—Treatment of lithium zirconium 9-*iso*propoxide *iso*propanolate (20 g.) with *tert.*-amyl alcohol followed by removal of *iso*propyl alcohol and excess of *tert.*-amyl alcohol left a brown liquid [Found: Zr, 20·6; Pr^iO, 26·8. $LiZr_2(OPr^i)_4(OCMe_2Et)_5$ requires Zr, 21·2; Pr^iO, 26·1%].

Disodium Trizirconium Oxydodecaethoxide.—(*a*) Zirconyl chloride octahydrate (100 g.), dissolved in ethyl alcohol (500 c.c.), was azeotropically dehydrated, benzene (80 c.c.) being used to form the tertiary azeotrope. More benzene (500 c.c.) was then added, and the solution treated with excess of ammonia. After separation of the ammonium chloride the filtrate was treated with a solution of sodium (7 g.) in alcohol (300 c.c.) and then fractionated to remove benzene, whereupon a white solid was precipitated. This was filtered off and twice recrystallised from toluene, giving large dense plates (44 g.) [Found: Na, 5·25; Zr, 31·3; EtO, 61·6. $Na_2Zr_3O(OEt)_{12}$ requires Na, 5·25; Zr, 31·2; EtO, 61·7%]. The *compound* was non-volatile up to 240°/0·5 mm. A sample (5 g.) was recrystallised ten times from toluene (500 c.c.) and gave large plates (3·5 g.) (Found: Na, 5·24; Zr, 31·5; EtO, 61·3%). (*b*) Zirconium oxide ethoxide (2·8 g.; EtO/Zr, 2·62) was treated with excess of alcoholic sodium ethoxide, and the solution concentrated to 40 c.c. The crystals produced were recrystallised from toluene and gave dense needles (1 g.) (Found: Na, 5·1; Zr, 31·7; EtO, 60·4%). (*c*) Zirconium oxide ethoxide (8 g.; EtO/Zr, 2·94) was likewise treated with excess of alcoholic sodium ethoxide and gave a precipitate (7 g.) which was recrystallised from toluene (400 g.), giving a crystalline product (5 g.) which was dried at 100°/0·5 mm. (Found: Zr, 31·3; EtO, 61·1%). The sodium zirconium oxydodecaethoxide was similarly obtained by starting with zirconium oxide ethoxides having ratios of EtO/Zr = 3·47 or 3·90.

Disodium Trizirconium Oxydodeca-n-*propoxide*.—Zirconium tetra-*n*-propoxide (10 g.) in *n*-propyl alcohol (200 c.c.) was treated with excess of propanolic sodium *n*-propoxide (40 c.c., N) and a white precipitate (4 g.) slowly appeared; this was separated and dried at 100°/0·5 mm. (Found: Na, 5·02; Zr, 26·0%). The substance recrystallised from boiling benzene (1·5% solution) in large dense plates [Found: Na, 4·34; Zr, 26·4. $Na_2Zr_3O(OPr^n)_{12}$ requires Na, 4·40; Zr, 26·2%].

*Disodium Dichlorodiiso*propoxycobaltate.—(*a*) Cobaltous chloride hexahydrate (14 g.) was dehydrated over a small flame, and the anhydrous salt dissolved in *iso*propyl alcohol. This solution, added to a solution of sodium (2·3 g.) in *iso*propyl alcohol (200 g.), caused immediate precipitation of a deep purple solid. After being refluxed for 10 min. the solid was filtered off and dried at 100°/0·5 mm. {Found: Na, 15·9; Co, 19·5; Cl, 24·5. $Na_2[CoCl_2(OPr^i)_2]$ requires Na, 15·6; Co, 20·1; Cl, 24·1%}. (*b*) Sodium zirconium ennea*iso*propoxide (5·8 g.) was refluxed

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for 10 min. with a solution of cobaltous chloride in *iso*propyl alcohol (31·7 c.c., 0·249N). The purple precipitate (1 g.) was dried at 100°/0·5 mm. (Found: Na, 14·9; Zr, 5·3; Co, 13·5; Cl, 23·5%). This substance was evidently $Na_2[CoCl_2(OPr^i)_2]$ contaminated with some zirconium *iso*propoxide. Evaporation of the foregoing filtrate gave a purple solid which was extracted

TABLE 4.

$Zr(OR)_4$		M(OR)				
R	Wt. taken (g.)	M	Normality	Req. (c.c.)	Calc. (c.c.)	M/Zr
Et	0·929 *	Na	0·111	14·99	15·40	0·487
,,	0·518 *	,,	,,	8·04	8·59	0·468
,,	4·165	,,	0·558	14·05	13·74	0·511
Pr^n	2·829	Na	0·901	5·05	4·79	0·527
Bu^n	6·218	Na	1·085	7·74	7·47	0·518
,,	2·938	,,	,,	3·65	3·53	0·517
Pr^i †	5·739	Na	0·0868	88·2	85·3	0·517
,,	4·415	,,	,,	67·0	65·7	0·511
,,	0·648	(NEt_4)	0·088	10·15	9·50	0·534
,,	2·645	,,	,,	41·3	38·8	0·532

* Ref. 1. † $Zr(OPr^i)_4$,Pr^iOH taken.

with benzene and left a purple residue but gave a practically colourless extract which was evaporated to dryness. The residue was recrystallised from *iso*propyl alcohol and the crystalline zirconium *iso*propoxide *iso*propanolate was dried at 20°/0·5 mm. [Found: Zr, 24·2; Pr^iO, 75·5. Calc. for $Zr(OPr^i)_4$,Pr^iOH: Zr, 23·5; Pr^iO, 76·2%].

Titrations.—The appropriate alcohol was used as solvent in all cases except that zirconium *iso*propoxide required the addition of some benzene to enhance its solubility. The alkali alkoxide solutions were prepared by dissolving in the alcohol a suitable weight of the metal, cut and weighed under benzene, under a guard tube filled with silica gel and pellets of potassium hydroxide. The titration assembly, consisting of a burette fitted into a titration flask with a grooved rubber bung, was similarly guarded. Solid indicator was used. The alkali alkoxide solutions were standardised against hydrochloric acid, potassium hydrogen phthalate, or benzoic acid. The results are presented in Table 4.

Molecular-weight Determinations.—Ebullioscopic measurements were made in a suitably

TABLE 5.

Compound	Range of *m* (g.)	Solvent	*T*/*m*	*M* Found	*M* Calc.
$LiZr_2(OEt)_9$	0·4786—2·963	EtOH	0·0603°	605	595
,,	0·1326—1·658	C_6H_6	0·0631	1240	,,
$NaZr_2(OEt)_9$	0·2419—1·101	,,	0·0955	820	611
$LiZr_2(OPr^n)_9$	0·2980—1·521	,,	0·0638	1230	721
$NaZr_2(OPr^n)_9$	0·3244—1·991	,,	0·0963	815	737
,,	0·3328—1·023	,,	0·0971	808	,,
$LiZr_2(OBu^n)_9$	0·2532—0·955	,,	0·0589	1330	847
$NaZr_2(OBu^n)_9$	0·3349—2·119	,,	0·0915	858	863
$KZr_2(OBu^n)_9$	0·2151—2·623	,,	0·0827	952	879
,,	0·2291—2·482	,,	0·0886	886	,,
$Zr_2(OPr^i)_8$,2Pr^iOH	0·4162—2·032	Pr^iOH	0·0611	773	775
$LiZr_2(OPr^i)_9$,Pr^iOH	0·3665—2·434	,,	0·0620	763	780
$LiZr_2(OPr^i)_9$,Pr^iOH	0·3172—1·136	C_6H_6	0·0883	763	,,
$LiZr_2(OPr^i)_9$	0·3864—1·204	,,	0·1033	760	721
$NaZr_2(OPr^i)_9$	0·1258—1·432	Pr^iOH	0·0701	681	737
,,	0·0692—0·9237	,,	0·0679	703	,,
,,	0·2009—1·261	C_6H_6	0·1066	725	,,
$NaZr_2(OPr^i)_9$ *	0·3227—1·940	Pr^iOH	0·0663	720	,,
,,	0·2337—1·859	C_6H_6	0·1007	767	,,
$(Et_4N)Zr_2(OPr^i)_9$	0·5978—1·211	,,	0·057	1380	844
,,	0·2400—1·745	Pr^iOH	0·0874	541	,,
$KZr_2(OPr^i)_9$	1·041 —1·814	C_6H_{12} †	0·079	904	879
$LiZr_2(OBu^s)_9$	0·6088—1·884	C_6H_6	0·0927	847	847
$LiZr_2(OEt)_4(OBu^t)_5$	0·3362—1·427	,,	0·1069	737	735

* Compound which had been stored for 3 months.
† *cyclo*Hexane, 43·4 c.c., *d* 0·776 g./c.c.; apparatus constant 28·6°/100 g. of solvent/mole of solute.

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adapted Menzies–Wright apparatus using a differential water-thermometer.[2] The same amount of solvent (40·0 c.c.), measured directly from a burette into the ebulliometer, was taken in each determination. The apparatus was calibrated for each solvent by using vacuum-distilled azobenzene. The following constants were obtained: Benzene, 31·4°, 31·4°; ethanol, 14·6°, 14·6°; *iso*propyl alcohol, 18·9°, 19·0°. The results are given in Table 5.

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76. *Experiments Relating to Phthiocerol. Part III.*[1] *Degradative Studies of a C_{11} Oxidation Product of Phthiocerol.*

By F. K. DRAYSON, J. W. LEWIS, and N. POLGAR.

New degradative evidence shows that the C_{11} methoxy-acid arising on oxidation of phthiocerol [2] is 7-methoxy-6-methylnonanoic acid (III); this structure has been proved by conversion of the methoxy-acid into 6-methyl-7-oxononanoic acid (V). The latter was synthesised *via* 4-methylhept-6-en-3-one (VIII) by addition of hydrogen bromide catalysed by peroxide, followed by condensation of the resulting bromide (IX) with ethyl sodiomalonate.

These and earlier results [2] indicate that phthiocerol is essentially 3-methoxy-4-methyl-*n*-tetratriacontane-9 : 11-diol (VI).

THE synthetical investigation reported in Part II [1] showed that the structure of the C_{11} methoxy-acid previously obtained [2] on oxidation of phthiocerol, and provisionally formulated as 6-methoxy-6-methylnonanoic acid (I), required revision. Degradative studies of the C_{11} methoxy-acid are now described.

In the earlier work, the C_{11} methoxy-acid was obtained in amounts which were insufficient for further studies. After various attempts to improve the isolation, the methyl ester of the C_{11} acid was obtained in reasonable yields by fractional distillation of the methyl esters of the crude mixture of acids resulting on oxidation of phthiocerol; the C_{11} acid is lævorotatory.

Demethylation of the C_{11} methoxy-acid with hot acetic anhydride–toluene-*p*-sulphonic acid (cf. Huffmann and Lott [3]) afforded a mixture of the corresponding acetoxy-acid and an unsaturated acid showing an infrared band at 966 cm.$^{-1}$ (*trans*-CH=CH). Under the same conditions, 6-methoxy-6-methylnonanoic acid [1] (I), possessing a tertiary methoxyl group, was demethylated to a product which did not absorb in the 966 cm.$^{-1}$ region; moreover, it contained no acetoxy-group. These comparative experiments indicated the presence of the grouping $\cdot CH_2 \cdot CH(OMe) \cdot$ in the C_{11} oxidation product.

When the methyl ester of the C_{11} oxidation product was treated with acetic anhydride and toluene-*p*-sulphonic acid under less vigorous conditions, it was converted into the acetoxy-ester which was hydrolysed to the corresponding hydroxy-acid. This was esterified, and then oxidised with chromic acid: the product consisted of an oxo-ester, together with unoxidised material. Hence the hydroxyl group must have been secondary.

(I) $CH_3 \cdot [CH_2]_3 \cdot CMe(OMe) \cdot [CH_2]_4 \cdot CO_2H$

(II) $CH_3 \cdot [CH_2]_{22} \cdot CH(OH) \cdot CH_2 \cdot CH(OH) \cdot [CH_2]_4 \cdot CMe(OMe) \cdot [CH_2]_3 \cdot CH_3$

The provisional formula (I) already mentioned for the C_{11} oxidation product of phthiocerol was based upon the structure (II) earlier suggested [2] for phthiocerol with the methoxyl and the methyl group both at $C_{(4)}$. Among the evidence advanced for this structure was the formation of a halogen-free product on refluxing phthiocerol with a solution of hydrogen bromide in glacial acetic acid, followed by treatment of the resulting bromo-derivative with zinc and sodium iodide in acetone; this suggested that removal

[1] Part II, Lewis and Polgar, *J.*, 1958, 102.
[2] Part I, Hall, Lewis, and Polgar, *J.*, 1955, 3971.
[3] Huffmann and Lott, *J. Biol. Chem.*, 1948, **172**, 789.

of the methoxyl group by the action of hydrogen bromide gave rise to an intermediate tertiary bromide which readily underwent elimination of the elements of hydrogen bromide during the above procedure. A tertiary bromide could also have arisen, however, by rearrangement during the demethylation according to the scheme

$$\cdot CHMe\cdot CH(OMe)\cdot \longrightarrow \cdot CMeBr\cdot CH_2\cdot$$

which is analogous to the known conversion of 1 : 2-dimethylpropyl alcohol by reaction with hydrogen chloride into 1 : 1-dimethylpropyl chloride.[4] On the basis of this interpretation, the earlier evidence [2] would also satisfy modifications of the structure (II) for phthiocerol in which the methoxyl group is placed at $C_{(3)}$ or $C_{(5)}$; the C_{11} oxidation product would then have structure (III) or (IV), respectively. A decision in favour of (III) was reached as follows:

(III) $CH_3\cdot CH_2\cdot CH(OMe)\cdot CHMe\cdot [CH_2]_4\cdot CO_2H$

(IV) $CH_3\cdot [CH_2]_3\cdot CHMe\cdot CH(OMe)\cdot [CH_2]_3\cdot CO_2H$

The oxo-ester obtained on oxidation of the demethylated product with chromic acid (see above) was hydrolysed, and the oxo-acid treated with acetic anhydride and sodium acetate under conditions known [5] to convert δ-oxo-acids into enol lactones; however, the infrared spectrum of the product showed the absence of enol-lactonic absorption, thus indicating that the acid was not a δ-oxo-acid. This argued against the presence of methoxyl in the δ-position of the parent-methoxy-acid as in formula (IV), and pointed to the alternative structure (III). The oxo-acid which resulted from the methoxy-acid by the procedures described is then 6-methyl-7-oxononanoic acid (V).

The work so far described (completed in 1956 [6]) indicated, therefore, that the formula (II) for phthiocerol requires a modification by moving the methoxyl group from $C_{(4)}$ to $C_{(3)}$; hence phthiocerol is 3-methoxy-4-methyltetratriacontane-9 : 11-diol (VI).

(V) $CH_3\cdot CH_2\cdot CO\cdot CHMe\cdot [CH_2]_4\cdot CO_2H$

(VI) $CH_3\cdot [CH_2]_{22}\cdot CH(OH)\cdot CH_2\cdot CH(OH)\cdot [CH_2]_4\cdot CHMe\cdot CH(OMe)\cdot CH_2\cdot CH_3$

In further experiments the oxo-ester, isolated with the aid of Girard's P reagent, was found to have $[\alpha]_D$ +2·2°, and to yield on alkaline hydrolysis optically inactive oxo-acid; evidently racemisation has taken place owing to the presence of the asymmetric centre adjacent to the oxo-group. Structure (V) was eventually confirmed by comparison of the oxo-acid and its ethyl ester 2 : 4-dinitrophenylhydrazone with synthetic specimens. 6-Methyl-7-oxononanoic acid (V) was synthesised as follows:

The acid chloride from 2-methylpent-4-enoic acid [7] (VII) with ethylzinc iodide gave 4-methylhept-6-en-3-one (VIII). This ketone, by addition of hydrogen bromide in presence of peroxide as catalyst, followed by treatment of the crude bromide (IX) with ethyl sodiomalonate, gave ethyl 2-ethoxycarbonyl-6-methyl-7-oxononanoate (X). Hydrolysis of the latter, followed by decarboxylation of the liberated acid, afforded 6-methyl-7-oxononanoic acid (V).

(VII) $HO_2C\cdot CHMe\cdot CH_2\cdot CH=CH_2$

(VIII) $CH_3\cdot CH_2\cdot CO\cdot CHMe\cdot CH_2\cdot CH=CH_2$

(IX) $CH_3\cdot CH_2\cdot CO\cdot CHMe\cdot [CH_2]_3\cdot Br$

(X) $CH_3\cdot CH_2\cdot CO\cdot CHMe\cdot [CH_2]_3\cdot CH(CO_2Et)_2$

Ryhage, Stenhagen, and von Sydow [8] have proposed structure (XI) for phthiocerol from mass spectrometric studies, whereas Demarteau-Ginsburg,[9] referring to the studies

[4] Whitmore and Johnston, *J. Amer. Chem. Soc.*, 1938, **60**, 2265.

[5] Woodward, Sondheimer, Taub, Heusler, and McLamore, *J. Amer. Chem. Soc.*, 1952, **74**, 4223; see also ref. 1.

[6] Lewis, D.Phil. Thesis, Oxford, 1956.

[7] Ställberg-Stenhagen, *Arkiv Kemi, Min., Geol.*, 1946, **23**, *A*, No. 15; Fray and Polgar, *J.*, 1956, 2036.

[8] Ryhage, Stenhagen, and von Sydow, *Acta Chem. Scand.*, 1957, **11**, 180.

[9] Demarteau-Ginsburg, *Compt. rend.*, 1956, **243**, 2169.

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of the Swedish investigators, suggests that phthiocerol is an approximately equimolecular mixture of compounds (VI) and (XI). These suggestions are not compatible with the formation of the C_{11} methoxy-acid as an oxidation product, and its conversion into 6-methyl-7-oxononanoic acid as shown above.

(XI) $CH_3 \cdot [CH_2]_{10} \cdot CH(OH) \cdot CH_2 \cdot CH(OH) \cdot [CH_2]_4 \cdot CHMe \cdot CH(OMe) \cdot CH_2 \cdot CH_3$

Experimental

Infrared spectra were determined on liquid films except where otherwise stated. Optical rotations were measured in a 0·5-dm. tube.

Isolation of the C_{11} Methoxy-acid and its Methyl Ester.—In the earlier work the following procedure was employed: chromium trioxide (6 g.) in water (6 c.c.) and glacial acetic acid (20 c.c.) was gradually added to phthiocerol (5 g.) in glacial acetic acid (40 c.c.), and the mixture heated on a steam-bath for 1 hr.; ethanol (10 c.c.) was then added to the cooled mixture. Most of the acetic acid was removed by distillation under reduced pressure, and the residue, after addition of dilute hydrochloric acid, was extracted with ether. Evaporation of the extract, followed by distillation of the product in steam, and isolation of the steam-volatile material by ether-extraction, gave the C_{11} methoxy-acid (0·31 g.), b. p. 190—200° (bath)/20 mm., n_D^{21} 1·4432, $[\alpha]_D^{17}$ −3·2° (*c* 4·22 in ether), −2·95° (*c* 9·50 in ether) (Found: C, 65·0; H, 10·5. Calc. for $C_{11}H_{22}O_3$: C, 65·3; H, 11·0%); infrared absorption: band at 1093 cm.$^{-1}$ (alkyl ether). More (0·2 g.) of the acid was obtained on distillation of the residue from the steam-distillation under reduced pressure.

Later the procedure was modified as follows: Phthiocerol (5 g.) in glacial acetic acid (200 c.c.) was heated on a steam-bath with chromium trioxide (6·2 g.) in water (75 c.c.) and acetic acid (75 c.c.) for 2 hr. The mixture was then poured into water and extracted with ether. After removal of the solvent and most of the acetic acid, the residue was esterified (with ethereal diazomethane or 3% methanolic sulphuric acid). Distillation gave the *methyl ester* of the C_{11} methoxy-acid (1·2 g., 61·5%), b. p. 118°/15 mm., n_D^{19} 1·4351 (Found: C, 66·5; H, 11·0. $C_{12}H_{24}O_3$ requires C, 66·7; H, 11·1%).

Demethylation of the C_{11} Methoxy-acid.—The methoxy-acid (0·32 g.) was heated on a steam-bath with acetic anhydride (10 c.c.) and toluene-*p*-sulphonic acid (0·12 g.) for 0·5 hr.; the mixture was then poured into water, and the whole heated on the steam-bath for 10 min. Ether-extraction followed by distillation gave a liquid (0·18 g.), b. p. 170—190° (bath)/20 mm. (Found: C, 67·3; H, 10·0. Calc. for $C_{12}H_{22}O_4$: C, 62·6; H, 9·6. Calc. for $C_{10}H_{18}O_2$: C, 70·6; H, 10·6%). The infrared spectrum showed bands at 966 (*trans*-CH=CH) and 1709 cm.$^{-1}$ (CO_2H), with a shoulder at 1739 cm.$^{-1}$ (OAc).

A specimen of 6-methoxy-6-methylnonanoic acid [1] similarly treated gave a liquid (Found: C, 71·1; H, 11·2%) whose infrared spectrum did not show bands due to methoxyl, acetoxyl, or *trans*-CH=CH groups.

Conversion of the C_{11} Methoxy-acid into an Oxo-acid.—The methyl ester (2·5 g.) of the C_{11} methoxy-acid was kept with acetic anhydride (200 c.c.) and toluene-*p*-sulphonic acid (0·65 g.) at room temperature for 40 hr., then poured into water. The resulting acetoxy-ester, isolated by ether-extraction, was hydrolysed by 1 hour's refluxing with potassium hydroxide solution (2 g. in 20 c.c. of water and 5 c.c. of ethanol). Acidification (hydrochloric acid) followed by ether-extraction gave the corresponding hydroxy-acid (the infrared spectrum of a distilled sample did not snow a band corresponding to lactonic carbonyl) which was converted, by means of ethereal diazomethane, into the methyl ester, b. p. 120—150° (bath)/10 mm., showing a strong band at 3390 cm.$^{-1}$ (OH). This ester (2 g.) in glacial acetic acid (20 c.c.) was kept with a solution of chromium trioxide (1 g.) in a little water and acetic acid (10 c.c.) at room temperature for 40 hr., then poured into water. An ethereal extract was washed with aqueous sodium carbonate and water, dried ($MgSO_4$), and evaporated. The resulting ketonic product was then separated with Girard-P reagent from non-ketonic material (containing, according to its infrared spectrum, unoxidised hydroxy-ester). The ketone fraction, obtained from the Girard-P extract by decomposition with 1N-sulphuric acid, followed by ether-extraction, had $[\alpha]_D^{18}$ +2·2° (*c* 12·2 in ether): its infrared spectrum showed carbonyl bands at 1715 (ketone) and 1739 cm.$^{-1}$ (ester). Hydrolysis of this oxo-ester by refluxing 5% aqueous-ethanolic potassium hydroxide for 0·5 hr., followed by acidification and ether extraction, gave the oxo-acid, b. p.

190—220° (bath)/9 mm., n_D^{18} 1·4530, which showed no measurable rotation. The infrared spectrum was in close agreement with that of a synthetic specimen of 6-methyl-7-oxononanoic acid. The 2 : 4-*dinitrophenylhydrazone* of the corresponding ethyl ester formed orange plates (from ethanol), m. p. 78° (Found: C, 54·7; H, 6·6; N, 14·2. $C_{18}H_{26}O_8N_4$ requires C, 54·8; H, 6·6; N, 14·2%) undepressed on admixture with ethyl 6-methyl-7-oxononanoate 2 : 4-dinitrophenylhydrazone.

In a small-scale experiment the oxo-acid (50 mg.) was refluxed with acetic anhydride (5 c.c.) and sodium acetate (50 mg.) for 20 hr. The infrared spectrum (in carbon disulphide) of the product showed a band at 1712 cm.$^{-1}$ (CO, CO_2H), but no band corresponding to a δ-enol lactone (1754 cm.$^{-1}$).

4-Methylhept-6-en-3-one (VIII).—A solution of oxalyl chloride (35 g.) and 2-methylpent-4-enoic acid [7] (27 g.) in benzene (50 c.c.), was kept at 35° for 3 hr.; the solvent and excess of oxalyl chloride were then removed under reduced pressure. The resulting acid chloride was caused to react, according to Blaise's method,[10] with a solution of ethylzinc iodide (from 150 g. of ethyl iodide, 100 c.c. of toluene, 25 g. of ethyl acetate, and 125 g. of zinc–copper couple), and the mixture worked up as described earlier for analogous cases.[11] Distillation gave *4-methylhept-6-en-3-one* (19 g., 64%), b. p. 152°, n_D^{15} 1·4322 (Found: C, 76·4; H, 11·0. $C_8H_{14}O$ requires C, 76·2; H, 11·1%). The 2 : 4-*dinitrophenylhydrazone* crystallised from ethanol as orange prisms, m. p. 57° (Found: C, 54·7; H, 5·7; N, 18·2. $C_{14}H_{18}O_4N_4$ requires C, 54·9; H, 5·9; N, 18·3%).

Ethyl 2-Ethoxycarbonyl-6-methyl-7-oxononanoate (X).—Hydrogen bromide was passed during 3 hr. into a solution of the preceding ketone (19 g.) in benzene (350 c.c.) in the presence of benzoyl peroxide (0·2 g.) and a few drops of water. The mixture was then washed with water, and the washings were extracted with ether; the combined organic liquids were dried ($MgSO_4$) and evaporated, to give the crude bromide (III). This was added to an ice-cold solution of ethyl sodiomalonate (from 25 g. of ethyl malonate, 3·7 g. of sodium, and 100 c.c. of ethanol), and the mixture was then refluxed for 0·5 hr. The product was poured into water, extracted with ether, and the extract washed, successively, with aqueous potassium carbonate, aqueous sodium thiosulphate, and water, then dried ($MgSO_4$), and evaporated. Distillation of the residue gave *ethyl 2-ethoxycarbonyl-6-methyl-7-oxononanoate* (16·7 g.), b. p. 179°/8 mm., n_D^{18} 1·4432 (Found: C, 62·7; H, 9·1. $C_{15}H_{26}O_5$ requires C, 62·9; H, 9·1%).

6-Methyl-7-oxononanoic Acid (V).—The malonic ester (16·7 g.) was refluxed with potassium hydroxide (10 g.) in water (200 c.c.) and ethanol (20 c.c.) for 2 hr. The resulting solution was acidified (hydrochloric acid), and the product, isolated by ether-extraction, decarboxylated at 170° (bath). The product was taken up in ether from which the acid was removed with 10% aqueous potassium hydroxide. The alkaline washings were then acidified (hydrochloric acid) and extracted with ether, and the dried ($MgSO_4$) extract evaporated. Distillation of the residue furnished *6-methyl-7-oxononanoic acid* (6·5 g.), b. p. 190—192°/16 mm., n_D^{18} 1·4534 (Found: C, 64·2; H, 9·5. $C_{10}H_{18}O_3$ requires C, 64·5; H, 9·7%). Treatment of the acid with Brady's reagent gave *ethyl 6-methyl-7-oxononanoate* 2 : 4-*dinitrophenylhydrazone*, m. p. 78—79° (from ethanol) (Found: C, 54·7; H, 6·8; N, 14·2. $C_{18}H_{26}O_8N_4$ requires C, 54·8; H, 6·6; N, 14·2%). This product was also obtained through the *ethyl ester*, n_D^{22} 1·4357 (Found: C, 66·9; H, 10·2. $C_{12}H_{22}O_3$ requires C, 67·3; H, 10·3%), prepared from the acid by means of 10% ethanolic sulphuric acid.

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[10] Blaise, *Bull. Soc. chim. France*, 1911, **9**, i—xxvi.
[11] Marks and Polgar, *J.*, 1955, 3851.

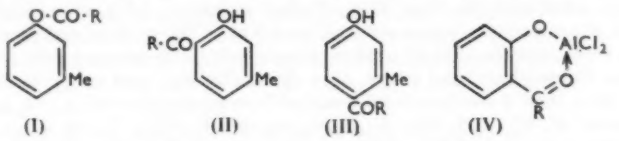
XUM

77. *The Fries Rearrangement. Part IV.* Study of the Reversibility of the Reaction.*

By N. M. Cullinane and B. F. R. Edwards.

Contrary to the results obtained by Rosenmund and Schnurr [1] *p*-hydroxy-ketones do not undergo the reverse Fries reaction, to give the corresponding esters, when treated with (+)-camphorsulphonic acid or similar reagents. While most of the original ketone is recovered, some scission takes place to the phenolic and acyl components; the components can then react, to give the *o*-hydroxy-ketone and in certain cases even acylate the hydroxyl group in the initial *p*-hydroxy-ketone.

It is generally accepted that, in the Fries rearrangement of phenol esters (cf. I) to hydroxy-ketones, formation of the *ortho*-isomer (II) tends to be favoured at high temperatures and that of the *para*-isomer (III) at low temperatures. It has therefore been suggested [2] that *para*-substitution, which is considered to be the more rapid reaction, is a reversible process, and that the ester re-formed in this way can then isomerise to the *o*-hydroxy-ketone, which is more stable owing to chelation with the catalyst, as indicated in (IV). The evidence on which these conclusions are based is, however, somewhat conflicting, and it has been shown that *o*-hydroxy-ketones are often formed at low temperatures, examples being provided in the transposition of phenyl [3] and *p*-tolyl [4] acetate and of *m*-tolyl propionate [5] and benzoate.[6,7] Moreover, migration to the *para*-position has also been observed at high temperatures, *e.g.*, for phenyl acetate [3] and phenyl [7] and *o*-tolyl benzoate.[1,8]



(I) (II) (III) (IV)

The chief experimental evidence in support of the reversibility of the Fries reaction is due to Rosenmund and Schnurr, who claimed that a number of *p*-hydroxy-ketones, including those derived from *m*-tolyl acetate, benzoate, and phenylacetate, and from thymyl and carvacryl acetate, can be converted, often in quantitative yield, into the initial esters by heating them with camphorsulphonic or sulphuric acid or a similar reagent. More recently Miguel, Müller, and Buu-Hoï [9] stated that many aliphatic esters of *m*-cresol were obtained in moderate yields by boiling the corresponding *p*-hydroxy-ketones with hydrochloric or hydrobromic acid.

The mechanism proposed for the Fries transposition in the present series of papers is based on the irreversibility of the *para*-isomerisation under the conditions examined and the results presented here are in agreement with this view. A quantitative study of the action of camphorsulphonic acid on the hydroxy-ketones cited by Rosenmund and Schnurr, under similar experimental conditions, shows that while most of the initial material is recovered some is split into its phenolic and acyl components. When concentrated

* Part III, *J.*, 1957, 3016.

[1] Rosenmund and Schnurr, *Annalen*, 1928, **460**, 56.

[2] Cf. Wheland, "Advanced Organic Chemistry," Wiley and Sons, New York, 1951, p. 565; Fieser and Fieser, "Organic Chemistry," Harrap and Co., Ltd., London, 1953, p. 676; Fuson, "Advanced Organic Chemistry," Wiley and Sons, New York, 1950, p. 346.

[3] Szekeres and Karsey, *Gazzetta*, 1947, **77**, 471.

[4] Cullinane and Edwards, *J.*, 1957, 3016.

[5] Baltzly and Bass, *J. Amer. Chem. Soc.*, 1933, **55**, 471; Coulthard, Marshall, and Pyman, *J.*, 1930, 280.

[6] Cox, *J. Amer. Chem. Soc.*, 1927, **49**, 1028.

[7] Unpublished results.

[8] Cox, *J. Amer. Chem. Soc.*, 1930, **52**, 352.

[9] Miguel, Müller, and Buu-Hoï, *Bull. Soc. chim. France*, 1956, 633.

sulphuric acid is substituted for the camphorsulphonic acid the decomposition is more extensive and nearly 60% of the cresol is obtained. Not more than a trace of the isomeric ester is formed in any of these reactions.

When the *p*-hydroxy-ketones were treated with hydrochloric acid, as in the method of Miguel *et al.*[9] (although they did not provide experimental details), the original ketone was almost entirely cleaved, to give the phenol: again we obtained none of the corresponding ester.

The acyl component resulting from scission of the *p*-hydroxy-ketone may be expected to attach itself to some extent to the *ortho*-position relative to the hydroxyl group by normal substitution, and we observed that small quantities of the *ortho*-isomer were obtained in some experiments. Moreover, acylation of the hydroxyl group should also be feasible and we found that small amounts of acylated *p*-hydroxy-ketones were sometimes formed.

According to Rosenmund and Schnurr the reversal does not take place if there is no alkyl group substituted in the *ortho*-position to the acyl substituent and our experiments with 4-hydroxy-3-methylacetophenone confirm this.

Experimental

Action of (+)-Camphor-10-sulphonic Acid on 4-Hydroxy-2-methylacetophenone.—The ketone was first obtained [10] by the action of acetyl chloride on *m*-cresol in contact with zinc chloride. We prepared it in 66% yield by heating *m*-tolyl acetate (0·1 mole, 15·0 g.) and anhydrous aluminium chloride (0·22 mole, 29·4 g.) in nitrobenzene (150 c.c.) for 24 hr. at 25°. The product was decomposed by ice and hydrochloric acid, the hydroxy-ketone extracted from the organic layer with 2N-sodium hydroxide, the extract acidified, and any of the *ortho*-isomer and *m*-cresol removed by distillation with steam, leaving the *p*-hydroxy-ketone [1,7,11] behind. This was filtered off and recrystallised from boiling water, as needles, m. p. 127°. The portion remaining in solution was converted into its 2 : 4-*dinitrophenylhydrazone*, which separated from aqueous alcohol in orange-red needles, m. p. 216° (Found: C, 54·5; H, 4·2; N, 17·0. $C_{15}H_{14}O_5N_4$ requires C, 54·5; H, 4·3; N, 17·0%).

(*a*) 4-Hydroxy-2-methylacetophenone (3 g.) and camphorsulphonic acid (0·006 g.) were heated at 150° for 30 min. under reflux, with exclusion of moisture. After being cooled, the mixture, which had an odour of acetic acid, became solid. It was dissolved in ether and extracted with 2N-sodium hydroxide. Traces of ether were removed by warming and the solution was then cooled, acidified with concentrated hydrochloric acid, and distilled with steam. After the addition of a little hydrochloric acid a slight excess of 2 : 4-dinitrophenylhydrazine reagent (containing 4 g. per 100 c.c. of concentrated sulphuric acid) was introduced and the whole set aside for 12 hr. The precipitated 2 : 4-*dinitrophenylhydrazone* of the *o*-hydroxy-ketone was washed successively with dilute hydrochloric acid and water and dried to constant weight at 110°. Recrystallisation from ethyl acetate yielded red prisms, m. p. 244° (Found: C, 53·9; H, 4·2; N, 16·9%). The filtrate from the hydrazone was cooled in ice, and excess of bromine water (10 g. of bromine and 15 g. of potassium bromide per 100 c.c. of water) was added gradually. After 1 hr. in the cold the 2 : 4 : 6-tribromo-*m*-cresol, m. p. 84°, was collected, washed with water, and dried. The residue from the steam-distillation, which contained the *para*-isomer, was filtered while hot through glass wool, and the residue extracted with boiling water, leaving a trace only of insoluble material. The product separated from the filtrate on cooling and was dried to constant weight. The small amount in solution was analysed by conversion into its 2 : 4-dinitrophenylhydrazone.

The results obtained were: recovered 4-hydroxy-2-methylacetophenone 91; 2-hydroxy-4-methylacetophenone 2; *m*-cresol 5·5%. No *m*-tolyl acetate was formed. In a similar experiment Rosenmund and Schnurr claimed a quantitative yield of this ester.

(*b*) The above experiment was repeated except that 0·03 g. of camphorsulphonic acid was used, with the following results: recovered 4-hydroxy-2-methylacetophenone 89; 2-hydroxy-4-methylacetophenone 1; *m*-cresol 8%.

(*c*) When concentrated sulphuric acid (0·1 g.) was substituted for camphorsulphonic acid

[10] Eijkman, *Chem. Weekblad*, 1904, **1**, 453.
[11] Baltzly, Ide, and Phillips, *J. Amer. Chem. Soc.*, 1955, **77**, 2522.

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and the mixture was heated for 30 min. at 180° a smell of acetic acid and considerable darkening were observed. The sole products obtained were: 4-hydroxy-2-methylacetophenone 37; 2-hydroxy-4-methylacetophenone 4; *m*-cresol 59%.

Action of (+)-Camphor-10-sulphonic Acid on 4-Hydroxy-2-methylbenzophenone.—(*a*) To anhydrous aluminium chloride (0·22 mole, 29·4 g.) in nitrobenzene (100 c.c.) at 0° *m*-tolyl benzoate (0·1 mole, 21·2 g.) in the same volume of nitrobenzene was added gradually, with stirring. The whole was heated at 60° for 13 hr., with stirring, then cooled in ice-water and treated with cold concentrated hydrochloric acid. The aqueous portion was extracted with ether, and the solution added to the nitrobenzene layer, which was next shaken with 10% sodium hydrogen carbonate solution (to dissolve the benzoic acid which was then precipitated by hydrochloric acid, dried, and weighed). Extraction of the organic layer with 2N-sodium hydroxide took up the *o*- and *p*-hydroxy-ketone and *m*-cresol, and acidification followed by steam-distillation removed the cresol and *o*-hydroxy-ketone which are volatile. The *o*-hydroxy-ketone separated on cooling, and was filtered off after being kept in the cold for 12 hr. Recrystallisation from alcohol and water gave pale yellow lustrous needles, m. p. 63°, as given by Baltzly *et al.*[11] The ketone remaining in solution was converted into the 2 : 4-*dinitrophenylhydrazone*, orange-red prisms (from ethyl acetate), m. p. 236° (Found: C, 60·6; H, 4·0; N, 14·2. $C_{20}H_{14}O_8N_4$ requires C, 61·2; H, 4·1; N, 14·3%). From the filtrate the *m*-cresol was precipitated in the usual way as the tribromo-derivative. The *p*-hydroxy-ketone,[11] which was present in the residue from the steam-distillation, was isolated by extraction with boiling water. It was deposited from aqueous alcohol in needles, m. p. 129°. The small amount in solution was converted into its 2 : 4-*dinitrophenylhydrazone*, red needles (from benzene), m. p. 224° (Found: C, 61·2; H, 4·0; N, 14·2%). From the organic layer, which contained any of the original *m*-tolyl benzoate and ketone esters, the ether was removed and the esters were hydrolysed for 8 hr. with boiling 6N-sodium hydroxide. When the nitrobenzene had been distilled with steam the residue was acidified and extracted with ether. Shaking with 10% sodium hydrogen carbonate solution took up the benzoic acid which was precipitated by hydrochloric acid. The ether solution, which now contained *m*-cresol (formed from the original ester) and the *o*- and *p*-hydroxy-ketone (formed from the ketone esters), was extracted with 2N-sodium hydroxide, and the products were analysed as described above.

Taking into account the small quantity of benzoic acid in solution, obtained by reference to solubility tables, we found: 4-hydroxy-2-methylbenzophenone 50·7; 2-hydroxy-4-methylbenzophenone 15·4; *m*-cresol 19·3; 4-benzoyl-3-methylphenyl benzoate 4·2; 2-benzoyl-5-methylphenyl benzoate 2·9; benzoic acid 25·0%; resin 0·3 g.

The benzoic acid formed was composed of that produced by the scission of the original *m*-tolyl benzoate (equivalent to the *m*-cresol), as well as that resulting from the hydrolysis of the other esters present in the products. The ketone esters were estimated by the analysis of their hydrolysis products only.

(*b*) Repetition of the experiment recorded by Rosenmund and Schnurr, in which *m*-tolyl benzoate (5 g.) and aluminium chloride (5 g.) were heated in nitrobenzene (30 g.) for 5 hr. at 60°, and in which they claimed as sole product (60%) the *p*-hydroxy-ketone, gave the following results: 4-hydroxy-2-methylbenzophenone 46·9; 2-hydroxy-4-methylbenzophenone, 9·2; *m*-cresol 25·4; 2-benzoyl-5-methylphenyl benzoate, 3·6; *m*-tolyl benzoate recovered 11·6; and benzoic acid 41%.

4-Hydroxy-2-methylbenzophenone (3 g.) and camphorsulphonic acid (0·03 g.) were heated at 150° for 30 min., then at 200° for 4 hr. N-Sodium hydroxide was added and dissolved all except a small quantity of solid. This was washed with more alkali and recrystallised from aqueous alcohol, giving colourless needles, m. p. 105°, of the benzoyl derivative [12] of the original hydroxy-ketone, identified by admixture with a specimen prepared from 4-hydroxy-2-methylbenzophenone. The alkaline filtrate was worked up in the usual way. The products were 4-hydroxy-2-methylbenzophenone (85·3%) and its benzoyl derivative (2·9%) together with *m*-cresol (5·7%) and a little resin (0·16 g.). No *m*-tolyl benzoate was formed, although this was the only product claimed by Rosenmund and Schnurr.

Action of (+)-Camphor-10-sulphonic Acid on Benzyl 4-Hydroxy-2-methylphenyl Ketone.—This compound was prepared by Blau [13] by treating a mixture of phenylacetic acid and *m*-cresol with zinc chloride. In our preparation powdered aluminium chloride (0·3 mole, 41 g.)

[12] Bartolotti, *Gazzetta*, 1900, **30**, 224.
[13] Blau, *Monatsh.*, 1905, **26**, 1149.

was added gradually to phenylacetyl chloride (0·13 mole, 20 g.) and *m*-cresol (0·13 mole, 14 g.) in nitrobenzene (100 c.c.), and the whole heated on a boiling-water bath for 30 min. The products, obtained by the usual method, consisted of the *p*-hydroxy-ketone (25·9%), needles (from aqueous alcohol), m. p. 142°, and *m*-cresol (9·2%), with some tar (6·3 g.).

The phenylacetyl-*m*-cresol (3 g.) was heated at 170° for 15 min. with camphorsulphonic acid (0·05 g.). The product had an odour of phenylacetic acid. When 0·5N-sodium hydroxide was added and the whole kept at 0° for 12 hr. a small amount of sticky solid remained undissolved; this was evidently mainly the phenylacetyl ketone ester since it gave the *p*-hydroxy-ketone (2·2%) on hydrolysis with alkali. The other products were the original ketone (87·3%) and *m*-cresol (4·1%). Unlike Rosenmund and Schnurr we obtained no *m*-tolyl phenylacetate.

Action of (+)-*Camphor*-10-*sulphonic Acid on* 4-*Hydroxy*-2-*methyl* 5-iso*propylacetophenone*.—The starting material was prepared by Rosenmund and Schnurr's method from thymol and acetyl chloride, in 97% yield, as needles (from aqueous alcohol), m. p. 125°. The 2 : 4-*dinitrophenylhydrazone* consisted of red needles (from alcohol), m. p. 189° (Found: C, 57·6; H, 5·4; N, 15·0. $C_{18}H_{20}O_8N_4$ requires C, 58·1; H, 5·4; N, 15·0%). No thymyl acetate was formed in the reaction.

The hydroxy-ketone (5 g.) was heated for 1 hr. at 180° with camphorsulphonic acid (0·05 g.). The mixture darkened somewhat and an odour of acetic acid was observed. The product, when cool, was treated with 0·5N-sodium hydroxide, a small quantity of sticky solid remaining undissolved; from this was obtained 1·6% of 4-*acetoxy*-2-*methyl*-5-iso*propylacetophenone*, needles (from aqueous alcohol), m. p. 49° (Found: C, 71·6; H, 7·6. $C_{14}H_{18}O_3$ requires C, 71·8; H, 7·7%). From the alkali-soluble portion thymol was isolated by taking advantage of its volatility in steam (the *p*-hydroxy-ketone was also slightly volatile; the amount in the steam-distillate was ascertained by precipitation as the 2 : 4-dinitrophenylhydrazone). In addition to the ketone ester there were obtained 75·1% of the initial ketone and 15·4% of thymol, but no thymyl acetate.

Action of (+)-*Camphor*-10-*sulphonic Acid on* 4-*Hydroxy*-5-*methyl*-2-iso*propylacetophenone*.—This compound was prepared by treating carvacrol (0·1 mole) and acetyl chloride (0·1 mole) in nitrobenzene (100 c.c.) with aluminium chloride (0·25 mole) at 25° for 24 hr. Of the products obtained the *p*-hydroxy-ketone (71%) was soluble in sodium hydroxide solution; the carvacryl acetate (16%) was hydrolysed, and the resulting carvacrol distilled with steam. The small quantity (2%) of acetoxy-ketone was estimated by hydrolysis. Although this ketone is slightly volatile in steam it is much less so than the carvacrol. Some tar (0·8 g.) was also produced. Recrystallisation of the main product from aqueous alcohol gave colourless needles, m. p. 101°. Rosenmund and Schnurr claimed a 90% yield of this substance and gave m. p. 120°, but John and Beetz [14] point out that the carvacrol used by the former authors was contaminated with thymol.

4-Hydroxy-5-methyl-2-*iso*propylacetophenone (3 g.) was heated with camphorsulphonic acid (0·03 g.) for 30 min. at 180°. Addition of 0·5N-sodium hydroxide to the cooled product left a small quantity of a sticky solid undissolved; this was mostly the ketone ester, for hydrolysis with 2N-sodium hydroxide yielded 4·9% of the hydroxy-ketone. The alkali-soluble portion contained the recovered ketone (69%) and carvacrol (21%).

Action of (+)-*Camphor*-10-*sulphonic Acid on* 4-*Hydroxy*-3-*methylacetophenone*.—The hydroxy-ketone II, 15 (3 g.) was heated for 30 min. at 150° with camphorsulphonic acid (0·03 g.). The product dissolved completely in 2N-sodium hydroxide. The yield of recovered ketone was 90·8%, and a little resin (0·2 g.) was also formed. No *o*-hydroxy-ketone, *o*-cresol, or *o*-tolyl acetate was formed.

Action of Hydrochloric Acid on 4-*Hydroxy*-2-*methylacetophenone*.—The ketone (5 g.) was boiled under reflux for 14 hr. with concentrated hydrochloric acid (50 c.c.). The product had an odour of acetic acid. Excess of N-sodium hydroxide was introduced with cooling and the whole shaken with benzene; no *m*-tolyl acetate was present in this layer. Traces of benzene were removed by heat from the aqueous portion which was then cooled, acidified with concentrated hydrochloric acid, and distilled with steam. The distillate contained a small quantity (0·4%) of 2-hydroxy-4-methylacetophenone (analysed by conversion into its 2 : 4-dinitrophenylhydrazone) and *m*-cresol (90·7%). Only 0·7% of the original hydroxy-ketone was recovered; it was estimated in the same way as its isomeric ketone.

[14] John and Beetz, *J. prakt. Chem.*, 1935, **143**, 342.
[15] Cullinane, Evans, and Lloyd, *J.*, 1956, 2222.

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Action of Concentrated Hydrochloric Acid on 4-Hydroxy-2-methylpropiophenone.—Propionyl chloride (0·3 mole, 27·8 g.), *m*-cresol (0·3 mole, 32·4 g.), aluminium chloride (0·66 mole, 88·0 g.), and nitrobenzene (300 c.c.) were stirred for 42 hr. at 15°. Working up in the usual way gave the *p*-hydroxy-ketone [5,8] (38·5%), m. p. 118°.

The above ketone (5 g.) was boiled under reflux for 14 hr. with concentrated hydrochloric acid (50 c.c.), and the products were extracted by a similar method to that described above. *m*-Cresol (94·9%) and the original ketone (2·1%) were the only compounds isolated. Miguel *et al.*[9], in a similar experiment, claimed a 39% yield of *m*-tolyl propionate.

One of us (B. F. R. E.) thanks the University of Wales for the award of a Post-graduate Studentship.

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78. *Nitryl Chloride. Part I. Its Preparation and the Properties of its Solutions in Some Organic Solvents.**

By M. J. COLLIS, F. P. GINTZ, D. R. GODDARD, E. A. HEBDON, and (in part) G. J. MINKOFF.

Nitryl chloride, NO_2Cl, was prepared by Dachlaucher's method as a pale yellow liquid, b. p. −14·3°, m. p. −141° ± 2°. Gaseous nitryl chloride decomposes at room temperature very slowly. The alkaline hydrolysis of nitryl chloride to hypochlorite and nitrite was confirmed. The nature of nitryl chloride in various organic solvents was studied as a preliminary to examining its reactions with organic compounds. Its solutions in less polar solvents are colourless, and those in polar solvents are yellow, the latter owing their colour to nitrosyl chloride and chlorine, formed by the hydrolysis of nitryl chloride by traces of moisture in these solvents. It also reacts with hydrogen chloride.

Preparation, Purification, and Physical Properties.—Although nitryl chloride was prepared [1] in 1929 by oxidation of nitrosyl chloride with ozone, its physical constants and the colour of the pure liquid are not yet accurately known. The more convenient method of preparation used here is the addition of chlorosulphuric acid to nitric acid at or just below room temperature: [2]

$$HSO_3Cl + HNO_3 \longrightarrow NO_2Cl + H_2SO_4$$

It was purified by passing ozonised oxygen through the liquefied gas to oxidise any nitrosyl chloride, then fractionally distilled to remove nitrogen dioxide and chlorine. Nitryl chloride condensed as a pale yellow liquid, b. p. −14·3°, and solidified to a pale yellow solid, m. p. −141° ± 2° (see Table 1).

Schumacher and Sprenger [1] and, later, Petri [3] reported that nitryl chloride condensed to a colourless liquid, but although the main impurities, chlorine, nitrogen dioxide, and nitrosyl chloride do colour the product, we found that the most careful refractionation does not remove its pale yellow colour. Its b. p. was constant within 0·2°, at any given atmospheric pressure, and its composition indicated that it was pure.

Ogg,[4] Seel,[5] and Volpe [6] and their co-workers purified nitryl chloride by vacuum distillation, but only Himel [7] used a low-temperature fractionating column which seemed

* For a summary of this work see *Chem. and Ind.*, 1955, 1742.

[1] Schumacher and Sprenger, *Z. anorg. Chem.*, 1929, **182**, 139.
[2] Dachlaucher, D.P. 509,405.
[3] Petri, *Z. anorg. Chem.*, 1948, **257**, 180.
[4] Ogg, Freiling, and Johnston, *J. Chem. Phys.*, 1952, **20**, 327.
[5] Seel and Nogradi, *Z. anorg. Chem.*, 1952, **269**, 188.
[6] Volpe and Johnston, *J. Amer. Chem. Soc.*, 1956, **78**, 3903.
[7] Himel, U.S.P. 2,511,915.

essential to remove chlorine. Dachlaucher [2] and Ville [8] both bubbled the gas through concentrated sulphuric acid to remove the oxides of nitrogen although we found that removal was not complete.

TABLE 1. *Physical constants of nitryl chloride; comparison with earlier work.*

Name	Method of Prepn.	Purifn.*	M. p.	B. p.	Analyses, etc.†
Schumacher and Sprenger [a]	$NOCl + O_2$	None	−145°	−15°	d_4^0 1·37, d_4^{16} 1·33
Petri [b]	$HNO_3 + HSO_3Cl$	None	−149	−15 to −14	d_4^{-20} 1·46
Batey and Sisler [c]	,,	None	−145	—	—
Seel and Nogradi [d]	,,	V.D.	−116	—	—
Shechter *et al.* [e]	,,	None	−145 ± 2	−17 to −15	44·9% Cl
Ville [f]	,,	None	—	−15	44—45% Cl
Present authors ...	,,	O_2 and F.D.	−141 ± 2	−14·3	17·07% N 43·6% Cl

* V.D., vacuum distillation; F.D., fractional distillation.
† Calc. for NO_2Cl: Cl, 43·52; N, 17·18%.
[a] Ref. 1; [b] ref. 3; [c] Batey and Sisler, *J. Amer. Chem. Soc.*, 1952, **74**, 3048; [d] ref. 5; [e] Shechter, Conrad, Daulton, and Kaplan, *J. Amer. Chem. Soc.*, 1952, **74**, 3052; [f] ref. 8.

Stability of Nitryl Chloride.—The kinetics of the thermal decomposition of nitryl chloride were studied by Schumacher and Sprenger,[9] who found that it decomposed at a measurable rate between 100° and 150°:

$$2NO_2Cl \longrightarrow 2NO_2 + Cl_2$$

Ogg and Wilson [10] showed that at room temperature chlorine and nitrogen dioxide interact slowly with the partial formation of nitryl chloride, an equilibrium being established. They gave no exact data for the extent or the rate of decomposition at room temperature except that nitryl chloride is considerably more stable than previously supposed. As we needed a clearer idea of its stability, we made some approximate measurements of the rate of decomposition of the gas at 25° by measuring the rate of increase of pressure. At room temperature one product of decomposition, nitrogen dioxide, is partially in the form of dinitrogen tetroxide, but it should be sufficiently dissociated to cause an appreciable rise in pressure with the decomposition of the nitryl chloride:

$$2NO_2Cl \longrightarrow (N_2O_4 \rightleftharpoons 2NO_2) + Cl_2$$

We concluded that dry nitryl chloride decomposes at approximately ½% per day, that moisture increases the rate, and that the decomposition is probably not photochemical. Despite the slow rate of decomposition, the initially colourless gas became distinctly brown in a few hours, presumably owing to traces of nitrogen dioxide.

Solutions of Nitryl Chloride in Organic Solvents.—Dilute solutions of nitryl chloride in polar solvents such as nitromethane, acetonitrile, and acetic acid were yellow whereas those in less polar solvents such as benzene, carbon tetrachloride, and methylene dichloride were colourless. The formation of colour was not always immediate, there often being an induction period of the order of minutes. The absorption spectra and distillation of these solutions showed that whereas colourless solutions contain pure nitryl chloride, the yellow colour is due to nitrosyl chloride and chlorine formed by hydrolysis by traces of water present in the more polar solvents:

$$3NO_2Cl + H_2O \longrightarrow NOCl + Cl_2 + 2HNO_3 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (I)$$

The only mode of hydrolysis of nitryl chloride previously reported [11] was under alkaline conditions when nitrite and hypochlorite are formed:

$$NO_2Cl + 2OH^- \longrightarrow NO_2^- + OCl^- + H_2O.$$

We confirmed this mode of hydrolysis by a better method.

[8] Ville, *Mem. Poudres*, 1955, **37**, 343.
[9] Schumacher and Sprenger, *Z. Electrochem.*, 1929, **34**, 653; *Z. phys. Chem.*, 1931, **12**, *B*, 115.
[10] Ogg and Wilson, *J. Chem. Phys.*, 1950, **18**, 900.
[11] Schmeisser and Gregor-Haschke, *Z. anorg. Chem.*, 1947, **255**, 34.

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Ultraviolet absorption spectra of solutions. In Table 2 the absorption maxima of solutions of nitryl chloride are compared with those of solutions of nitrosyl chloride.

TABLE 2. *Ultraviolet maxima of solutions of nitryl chloride and nitrosyl chloride in various solvents.*

Solvent	NO_2Cl				NOCl			
	λ (mμ)	ε	λ (mμ)	ε	λ (mμ)	ε	λ (mμ)	ε
Coloured solutions								
$MeNO_2$	373	9·8	460	3·5	373	17·3	460	10·5
$EtNO_2$	370	14·4	460	4·2	370	20·7	460	10·7
$Me{\cdot}CO_2H$	248	1120	460	3·4	248	2820	460	11·6
MeCN	222	3390	460	3·4	221	8760	460	9·8
Ac_2O	—	—	460	2—9 *	—	—	450	8·5
AcOEt (0·023% H_2O)	252	—	460	4·1	—	—	—	—
Colourless solutions								
CCl_4	258	250	—	—	258	420	460	12·8
CH_2Cl_2	No max. above 230				No lower max.		470	10·0
AcOEt (anhyd.)	252	317			252	962	460	9·7

* Beer's law not obeyed; ε = 9·3 at 0·015M, ε = 2·0 at 0·22M.

Nitrosyl chloride solutions are characterised by an absorption band at 460 mμ to which they owe their yellow colour. The fact that coloured nitryl chloride solutions also show a maximum at this wavelength and that the extinction coefficient is approximately one third that of pure nitrosyl chloride is consistent with the hydrolysis (1).

The absorption band at *ca.* 370 mμ of solutions in nitromethane and nitroethane is characteristic of the solvent rather than the solute; it appeared with solutes as diverse as chlorine, dinitrogen tetroxide, and ethylamine, but since it was not found with solutions of acids such as nitric, sulphuric, hydrochloric, and acetic it is probably associated with an anionic form of the nitro-alkane, although the nitromethane ion $CH_2NO_2^-$ absorbs at 234 mμ in aqueous solution.[12]

The water content of solvents. In acetonitrile, nitromethane, and nitroethane Beer's law was obeyed where the concentration was 0·05M or below. Above this, the extinction coefficient for the maximum at 460 mμ decreased, suggesting that there was then insufficient water present for complete reaction; when water was added to 0·195M-nitryl chloride in acetonitrile, the extinction coefficient rose from 1·5 to 3·1. It is to be expected that these solvents should contain just sufficient water to hydrolyse 0·05M-nitryl chloride, *i.e.*, they should be M/60 in water (0·03% w/v). Table 3 shows that some batches of solvent used contained less than this. Presumably additional water was collected from the atmosphere when the solution was made.

TABLE 3. *Water content of solvents* (% H_2O *w/v*).

Coloured nitryl chloride solutions		Colourless nitryl chloride solutions	
Acetic acid	0·049, 0·048	Benzene	0·018
,, (boron acetate dried)	0·023, 0·051	Benzene (sodium dried)	0·0022
Acetonitrile	0·025	Carbon tetrachloride	0·0057
Ethyl acetate	0·023, 0·036	Ethyl acetate	0·0088
Nitroethane	0·014, 0·076	Methylene dichloride	0·012
Nitromethane	0·013, 0·091		
	0·021, 0·101		

Rate of coloration of nitryl chloride solutions. Since the solvents forming colourless solutions were not perfectly dry, hydrolysis of nitryl chloride cannot be solely dependent on the water content. Nitryl chloride is apparently not so readily hydrolysed in the less polar solvents. The rate of appearance of colour in an initially colourless solution in nitromethane is autocatalytic (see Fig. 2; note that the absorptions at 373 and 460 mμ

[12] Kortum, *Z. phys. Chem.*, 1939, **43**, *B*, 271.

increased simultaneously). The induction period varied with the conditions; rise in temperature or addition of polar substances such as quaternary ammonium salts and nitric acid shortened it. Solutions in acetonitrile showed a similar induction period of a few minutes, but in acetic acid the colour appeared immediately. With ethyl acetate the induction period was often very long (1—3 hr.).

FIG. 1. *Ultraviolet spectra in nitromethane of A*, 0·028M-NOCl; *B*, 0·026M-Cl_2; *and C*, 0·030M-NO_2Cl.

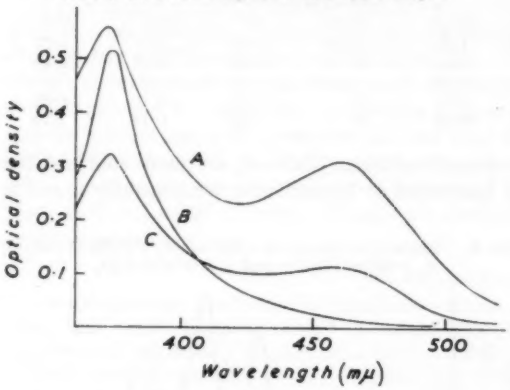
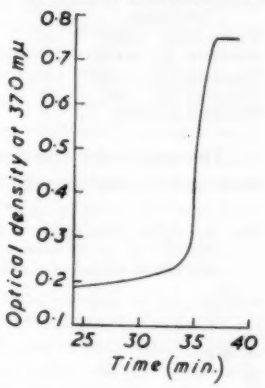


FIG. 2. *Rate of development of colour in nitryl chloride solutions in nitromethane.*



Infrared absorption spectra. The infrared absorption spectrum of the vapour above a concentrated solution of nitryl chloride in nitromethane (Table 4) shows that the vapour contained, as expected, bands due to nitryl chloride, nitrosyl chloride, and nitromethane.

TABLE 4. *Infrared absorption frequencies (cm.$^{-1}$) of the vapour above various systems; comparison with earlier work (medium resolution).*

NO_2Cl [a]	NO_2Cl in $MeNO_2$ [a]	NOCl in $MeNO_2$ [a]	Pure $MeNO_2$ [a]	NO_2Cl [a]	NOCl [b]	Comments
—	1795 s	1795 s	—	—	1800 vs	Presence of NOCl
1680 m	1700 m	—	—	1685 vs	—	Presence of NO_2Cl
—	1610 vs	1610 vs	1610 vs	—	—	
—	1390 s	1390 s	1390 s	—	—	
1321 s, 1287 s	1300 m	—	—	1318 vs, 1293 vs	—	Presence of NO_2Cl
—	930 s	930 s	930 s			
—	910 s	910 s	914 s	—	921 s	
—	900 s	900 s	905 s			
800, 790 vs, 780	794 vs	780 m	790 w	794 vs	—	Presence of NO_2Cl

[a] These measurements were made in the Chemical Engineering Department of Imperial College, London, S.W.7.

[a] Ryason and Wilson, *J. Chem. Phys.*, 1954, **22**, 2000; [b] Wise and Elmer, *ibid.*, 1950, **18**, 1411.

Vacuum distillation of nitryl chloride solutions. The hydrolysis of nitryl chloride in the yellow solutions was confirmed by the vacuum distillation at room temperature of solutions of nitryl chloride in various solvents. The distillate was initially condensed out in a trap (3) cooled to −80°, and the volatile components were then distilled off and separated into a more volatile early fraction (1) and a second later fraction (2), both of which were condensed −180°. All fractions were finally hydrolysed and analysed for total acid, Cl^-, OCl^-, and NO_2^-. Examples of the results are given in Tables 5 and 6.

Nitryl chloride distils almost unchanged from colourless solutions (Table 5), the hydrolysed distillates containing approximately equivalent amounts of nitric and hydrochloric

acids. The small amounts of nitrous acid found were attributed to slight decomposition of the nitryl chloride. The results thus support the view that colourless solutions contain pure nitryl chloride.

TABLE 5. *Distillation of a colourless solution.*

Solvent, C_6H_6; initial concn., NO_2Cl = 0·049M (total 2·96 mmoles); 91% of Cl^- distilled.

Products (mmoles)	OCl^-	Cl^-	NO_2^-	NO_3^-
Pump trap, −180°	0	1·41	0·02	1·37
Receiver (1), −180°	0	0·53	0·01	0·54
Receiver (2), −180°	0	0·17	0·09	0·16
Receiver (3), −80°	0	0·30	0	0·39
Residual solution ...	0	0·29	0·06	0·43

TABLE 6. *Distillation of a coloured solution.*

Solvent, Me·CO_2H; initial concn., NO_2Cl = 0·086M (total 4·30 mmoles); 86% of Cl and 44% of N distilled.

OCl^-	Cl^-	NO_2^-	NO_3^-
0·30	2·85	0	1·27
0	0·30	0·02	0·48
—	—	—	—
0	0·18	0	0·80
0	0·60	0·14	2·29

The results for the distillation of coloured solutions (Table 6) are more confused but show a few clear trends. First, small quantities of hypochlorite are generally found in

FIG. 3. *Effect of addition of hydrogen chloride to a solution of nitryl chloride in methylene dichloride.*

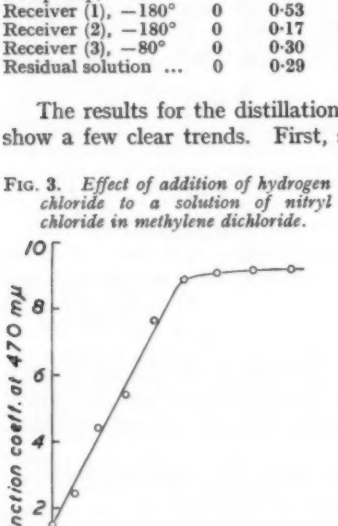
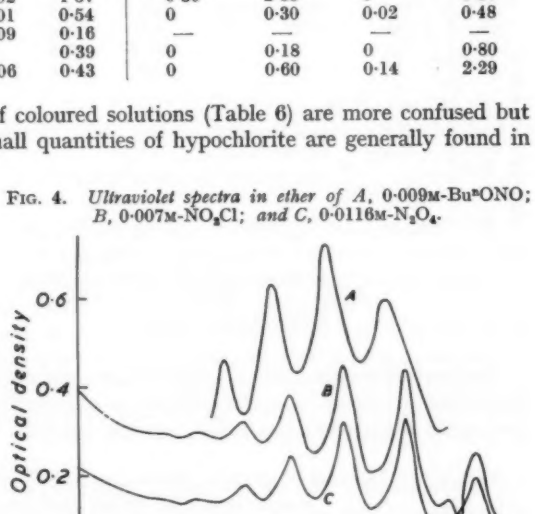


FIG. 4. *Ultraviolet spectra in ether of A, 0·009M-Bu^{n}ONO; B, 0·007M-NO_2Cl; and C, 0·0116M-N_2O_4.*



the hydrolyses of initial fractions or in the pump trap. Secondly, the concentration of chloride in the hydrolysed distillate is much greater, often by a factor of 2 or 3, than that of the nitrate.

These results are those expected for the distillation of a solution containing nitrosyl chloride and chlorine if, under vacuum, the nitrosyl chloride and chlorine largely distilled together; the hydrolysis products would then be a mixture of 3 equiv. of chloride to 1 of nitrate:

$$NOCl + Cl_2 + 2H_2O \longrightarrow HNO_3 + 3HCl.$$

Effect of Acids on Solutions of Nitryl Chloride in Nitromethane.—Sulphuric acid. The addition of sulphuric acid, like that of chlorosulphuric and perchloric acids, reduced the intensity of the yellow colour. When sulphuric acid was added to a concentrated solution of nitryl chloride in nitromethane, colourless crystals separated which redissolved on further addition of the acid. Analysis showed them to be nitrosonium hydrogen sulphate ($NO^+ \cdot HSO_4^-$).

Hydrochloric acid. Hydrochloric acid, unlike sulphuric acid, enhances the absorption of yellow solutions. The extinction coefficient of the absorption maximum at 460 mμ rose from 3·5 to 5·1. We are unable to explain this.

The Reaction of Nitryl Chloride with Hydrogen Chloride.—When hydrogen chloride was bubbled into liquid nitryl chloride at −40° there was exothermic formation of chlorine and nitrosyl chloride. The equation

$$NO_2Cl + 2HCl \longrightarrow NOCl + Cl_2 + H_2O$$

was shown to be correct by observing the absorption spectrum of a solution of nitryl chloride in methylene dichloride to which increasing quantities of hydrogen chloride were added (Fig. 3).

The Reaction of Nitryl Chloride with Ether.—Although dilute solutions of nitryl chloride in ether were colourless, their ultraviolet absorption spectra differed markedly from those of colourless solutions in other solvents (Fig. 4). The series of maxima observed at 330—400 mμ were identical with the spectrum of dinitrogen tetroxide in ether [13] and characteristic of a nitrite ester.[14] There was no evidence of appreciable reaction between nitryl chloride and the solvent since the spectrum did not vary with time and equivalent quantities of nitric and hydrochloric acids were produced by hydrolysis. However, when concentrated nitryl chloride (2M) in ether was kept between 0° and +5° an exothermic reaction took place with reduction of nitryl chloride to nitrosyl chloride and formation of oxidation products of ether.

Experimental

Preparation and Purification of Materials.—Nitric acid was rendered anhydrous by vacuum distillation from sulphuric acid.[15] *Fractional distillation of nitryl chloride.* Crude nitryl chloride was fractionally distilled in a column 75 cm. long packed with Fenske glass helices. A small amount of chlorine (b. p. −34°) generally distilled first, then nitryl chloride which was obtained as a pale yellow liquid, b. p. −14·3°. A small residue, containing mainly nitryl chloride and some dinitrogen tetroxide, was left. The b. p. of nitryl chloride was measured with a thermocouple junction enclosed in a glass capillary in the top of the column. The f. p. was measured with the apparatus shown in Fig. 5. The thermocouple leads were encased in a narrow glass tube filled for several inches with mercury to counter the conduction of heat down the leads. The usual cooling curve was plotted.

Analysis of Nitryl Chloride.—An ampoule containing a known weight of nitryl chloride was smashed under carbon tetrachloride which was covered by a layer of 6N-potassium hydroxide. After being shaken, the aqueous layer was separated and added to the washings of the organic layer. Portions of this solution were analysed for hypochlorite by electrometric titration with arsenite and for nitrogen by Devarda's method. The total chloride was determined gravimetrically as silver chloride after acidification, which allowed the nitrite to reduce the hypochlorite to chloride; independent experiments showed that nitrite and hypochlorite interact rapidly in acid or neutral solution but are stable in solutions $\geqslant$0·1N in alkali.

Nitromethane.—Prepared from sodium nitrite and sodium chloroacetate,[16] it was dried ($CaCl_2$) and last traces of water were removed by fractionation since water forms a lower-boiling azeotrope with nitromethane. Since Karl Fischer titration showed the solvent to be still slightly moist, drying with phosphoric oxide was tried but as the water content was only slightly reduced and much nitromethane was lost this treatment was generally omitted.

Some samples of the purified solvent gave solutions of nitryl chloride showing abnormal absorption spectra, apparently owing to an impurity probably produced by thermal decomposition of the nitromethane during fractionation. Careful refractionation under reduced pressure at 60° failed to remove it, but it was eventually removed by shaking with activated alumina for 10 min., decanting, and rapidly distilling. The infrared spectrum of the impure nitromethane was compared with that of the pure material, but no difference could be detected presumably because the concentration of the impurity was too small. We thank Dr. V. S. Griffiths (Battersea Polytechnic) for assistance with these infrared measurements.

Nitroethane.—Purified as for nitromethane, it contained a similarly troublesome impurity which affected the absorption spectra of nitryl chloride solutions; this was removed with alumina.

[13] Ungnade and Smiley, *J. Org. Chem.*, 1956, **21**, 993.
[14] Haszeldine, *J.*, 1953, 2525.
[15] Hughes, Ingold, and Reed, *J.*, 1950, 2438.
[16] *Org. Synth.*, 2nd edn., Vol. I, p. 401.

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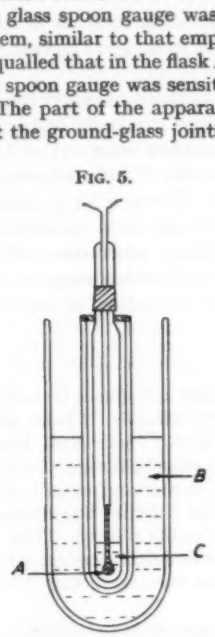
Other organic solvents were purified by standard methods.

Rate of Decomposition of Nitryl Chloride.—The apparatus is shown in Fig. 6. Nitryl chloride was allowed to distil through phosphoric oxide into the glass reaction vessel *F*. When the pressure reached 600 mm., tap T_1 was closed, the nitryl chloride in *F* frozen in liquid air, and the flask sealed off at *S*. The flask and spoon gauge were immersed in a thermostat at 25°. The glass spoon gauge was used as a null-point instrument, the tube *P* being connected to a system, similar to that employed by Kabesh and Nyholm,[17] for varying the pressure at *P* until it equalled that in the flask *F*. The absolute pressure was then read from a mercury manometer. The spoon gauge was sensitive to less than 1 mm. difference in pressure.

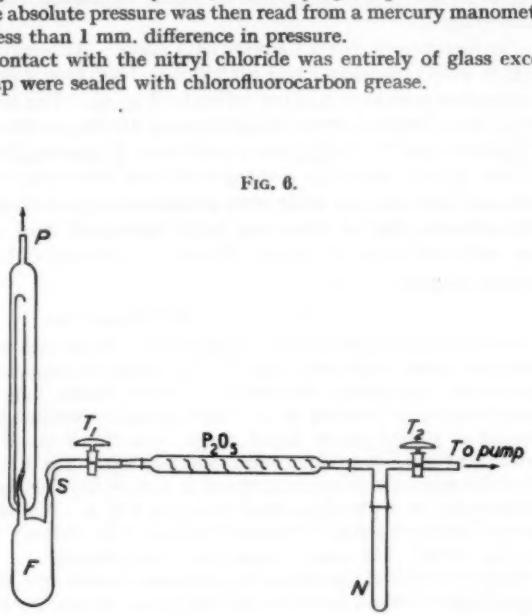
The part of the apparatus in contact with the nitryl chloride was entirely of glass except that the ground-glass joints and tap were sealed with chlorofluorocarbon grease.

FIG. 5.



A, Mercury–thermocouple junction; *B*, liquid air; *C*, liquid nitryl chloride.

FIG. 6.



When the rate of decomposition of moist nitryl chloride was determined the reaction flask *F* was filled initially with water vapour at 5 mm. pressure by means of an ancillary connection which was then sealed off.

Ultraviolet Spectroscopy.—The absorption spectra of solutions were determined by the Unicam S.P.500 Spectrophotometer. Stoppered silica cells, of 10 mm. optical path-length, were used.

Solutions of nitryl chloride were generally prepared by the rapid transfer of liquid nitryl chloride from the storage tubes to the solvent with a pipette, although some were made by distillation of nitryl chloride through phosphoric oxide directly into the solvent. The concentration of these solutions was determined by hydrolysing a sample and determining the chloride by Mohr's method, except for solutions in acetic acid and acetonitrile when Volhard's method was used.

Analysis of the Products of the Vacuum Distillation of Solutions of Nitryl Chloride.—Nitrite was determined by the standard method by use of either chloramine-T or ceric sulphate, and hypochlorite by titration with thiosulphate, and chloride as above. Nitrate was estimated by difference by titrating the total acid with alkali or, when acetic acid was the solvent, by reduction of the total nitrogen to ammonia. In the acid–alkali titration either methyl-red or bromocresol-green was used as the indicator, although when nitroethane was the solvent the end-point was determined potentiometrically.

Reaction between Sulphuric Acid and Nitryl Chloride in Nitromethane.—Sulphuric acid was

[17] Kabesh and Nyholm, *J.*, 1951, 3249.

added dropwise to 100 ml. of 0·5M-nitryl chloride in nitromethane until no more solid was deposited. The solid was filtered off on a sintered glass plate, washed twice with small portions of nitromethane, and dried *in vacuo* [Found: equiv., 43·2; NO^+ (chloramine-T), 18·7%. Calc. for $NO{\cdot}HSO_4$: equiv., 42·3; NO^+, 23·6%]. Some nitrous acid was probably lost in the hydrolysis.

Reaction of Nitryl Chloride with Hydrogen Chloride.—The volatile products of the reaction were distilled off at room temperature and condensed in a trap at −80°. The residue was a pale yellow liquid which analysis showed to be an aqueous solution of nitric and hydrochloric acids containing a trace of nitrous acid. The volatile product was fractionally distilled and separated into (*a*) a yellow liquid, b. p. −30° (cf. Cl_2, b. p. −33°); a weighed portion was dissolved in carbon tetrachloride and the solution mixed with aqueous iodide and titrated with thiosulphate (Found: Cl_2, 98·3%), and (*b*) a cherry-red liquid, b. p. −5° (cf. NOCl, b. p. −6°); a weighed portion was hydrolysed and total acid and chloride determined (Found: equivalent, 35·3; Cl, 50%. Calc. for NOCl: equiv., 32·7; Cl, 54%).

Reaction of Nitryl Chloride with Ether.—The cherry-red mixture was fractionally distilled. Ether containing almost pure nitrosyl chloride (in over 50% yield) distilled first leaving a residue which distilled in the range 70—160°. Chemical tests and the b. p. indicated that ethyl alcohol, ethyl acetate, acetic acid, formic acid, and probably chloroacetic acid were present.

The authors thank the Governors of Chelsea Polytechnic for a research assistantship (to M. J. C.).

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79. *Nitryl Chloride. Part II.* The Reaction with Alkylbenzenes.*

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Nitryl chloride, in various solvents at room temperature and below, chlorinates (rather than nitrates) toluene, *m*- and *p*-xylene, and mesitylene, although not benzene. The extent of chlorination was measured and the products isolated.

With polar solvents, in which nitryl chloride forms yellow solutions, the chlorinating agent is probably free chlorine produced by the reaction of nitryl chloride with traces of water. With the less polar solvents, in which nitryl chloride forms colourless solutions, it is probably the nitryl chloride molecule itself.

The kinetics of chlorination in nitromethane–ether were studied by dilatometric and chemical techniques. With the aromatic compound in excess, the reaction velocity was of the first order. The rate increased markedly with increase in the reactivity of the hydrocarbon and with increase in the polarity of the solvent. These facts are consistent with a mechanism involving a bimolecular attack by a chlorine molecule on the aromatic compound.

THE formula of nitryl chloride, NO_2Cl, suggests that it could either nitrate or chlorinate aromatic compounds. Gillespie and Millen [1] predicted the following series of nitrating agents of increasing power, on the basis that the efficiency of $X{\cdot}NO_2$ depends on the electron affinity of X: $EtO{\cdot}NO_2 < HO{\cdot}NO_2 < AcO{\cdot}NO_2 < NO_3{\cdot}NO_2 < Cl{\cdot}NO_2 < H_3O^+{\cdot}NO_2 < NO_2^+$. The order is also that of the increasing strength of the acid HX. They expected, therefore, that nitryl chloride should be a very reactive nitrating agent, even more powerful than dinitrogen pentoxide. Similarly, chlorinating agents could be arranged in order of reactivity, the efficiency of the agent $Y{\cdot}Cl$ increasing with the electron

* Part I, preceding paper.

[1] Gillespie and Millen, *Quart. Rev.*, 1948, **2**, 277.

affinity of Y and hence with the strength of the acid HY: $HO{\cdot}Cl < AcO{\cdot}Cl < NO_2{\cdot}Cl < Cl{\cdot}Cl < H_2O^+{\cdot}Cl < Cl^+$. Thus nitryl chloride should be a moderate chlorinating agent, slightly weaker than molecular chlorine.

Steinkopf and Kuhnel,[2] who first studied the reaction of nitryl chloride with organic compounds, found that at room temperature nitryl chloride dissolved in benzene without reacting, and that when warmed the nitryl chloride evaporated off unchanged. When benzene and nitryl chloride were heated under pressure 1-chloro-2-nitro*cyclo*hexadiene was formed which decomposed producing nitrobenzene. Nitryl chloride reacted violently with naphthalene, forming both 1-nitro- and 1-chloro-naphthalene.

However, Price and Sears [3] reported that nitryl chloride reacts with benzene at room temperature to form nitrobenzene, although in only 30% yield, and that the nitrating action of nitryl chloride was enhanced by the presence of Lewis acids, *e.g.*, aluminium trichloride, in presence of which and in carbon disulphide as solvent benzene gave a 90% yield of nitrobenzene and toluene a mixture of *o*- and *p*-nitrotoluene in yields of 47 and 24% respectively. Similarly, naphthalene gave 1-nitronaphthalene in 31% yield.

We confirmed Steinkopf and Kuhnel's observation for benzene. The formation of nitrobenzene reported by Price and Sears [3] might have been caused by catalysis by impurities such as nitrogen dioxide or nitric acid. We could not confirm the formation of 1-chloro-2-nitro*cyclo*hexadiene when nitryl chloride and benzene are heated together, but only detected nitrobenzene.

The reaction of nitryl chloride with various alkylbenzenes was studied. At room temperature or below, it forms with toluene, *p*-xylene, and mesitylene chloro-derivatives, with little or no nitro-derivatives. The kinetics of chlorination were studied.

Extent of Chlorination and Nitration of Alkylbenzenes by Nitryl Chloride.—This work was mostly done before that on the nature of nitryl chloride solutions reported in Part I, the observation during it of the yellow colour of solutions of nitryl chloride in nitromethane leading to their study.

The alkylbenzene (*p*-xylene or mesitylene) was added to a cooled solution of nitryl chloride in the solvent. The course of the reaction was followed by withdrawing samples of the reaction mixture, hydrolysing them, and determining the chloride and total acid. The relative proportions of chlorination and nitration were determined by using a known amount of nitryl chloride with the alkylbenzene in excess and then estimating the quantity of organic chloro- and nitro-compounds produced. The extent of nitration, based on the initial nitryl chloride concentration, was never more than 3·5%. The results for chlorination given in Table 1 are typical.

TABLE 1. *Extent of chlorination of alkylbenzenes during* 3 *hr.*

[ArH] (in excess), 0·2—2·0 moles/l.; [NO_2Cl], 0·05—0·40 mole/l.

Temp.	Aromatic cpd.	Solvent	Chlorination (%) * Total	Side-chain	Temp.	Aromatic cpd.	Solvent	Chlorination (%) * Total	Side-chain
0°	Toluene	$MeNO_2$–Et_2O (2 : 1)	40	—	−5°	Mesitylene	$MeNO_2$	55	—
					20	,,	,,	55	14
					20	,,	$Me{\cdot}CO_2H$	51	—
0	*p*-Xylene	,,	50	—	20	,,	MeCN	56	—
−5	,,	$MeNO_2$	57	—	20	,,	C_6H_6	60	—
20	,,	,,	51	11	20	,,	,,	63	23
20	,,	$Me{\cdot}CO_2H$	52	—	20	,,	$Me{\cdot}CO_2Et$	61	—
					20	,,	,,	65	30
					20	,,	CH_2Cl_2	65	—

* Based on initial concn. of NO_2Cl.

The products isolated are given in Table 2 for solutions in nitromethane (*n.i.*, not isolated; *d*, isolated as a derivative).

[2] Steinkopf and Kuhnel, *Ber.*, 1942, **75**, 1323.
[3] Price and Sears, *J. Amer. Chem. Soc.*, 1953, **75**, 3276.

TABLE 2.

Hydrocarbon:	*p*-Xylene	Mesitylene
Hydrocarbon in excess	2-Chloro- and 2-nitro-*p*-xylene	Nitro(*n. i.*) and chloro-mesitylene
Nitryl chloride in excess	2 : 5-Dichloro- and 2-nitro-*p*-xylene (*d*)	Trichloromesitylene

The Nature of the Chlorinating Agent.—(a) *Coloured solutions of nitryl chloride in nitromethane.* In Part I it was shown that these solutions were yellow owing to the hydrolysis of nitryl chloride by traces of moisture in the solvent:

$$3NO_2Cl + H_2O \longrightarrow NOCl + Cl_2 + 2HNO_3 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

The reaction, which takes place only after an induction period of several minutes, is complete in solutions of strength of the order 0·05M. By comparing the action of an initially colourless solution with a coloured one, we showed that the coloration corresponds with the formation of a very reactive chlorinating agent which can only be chlorine itself.

If chlorine were the sole chlorinating agent in these solutions we should not expect the extent of chlorination to exceed one third. Yet in practice the percentage of chlorination in 2—3 hr. is of the order of 55. A careful check of the extent of chlorination against reaction time revealed that the initial rapid reaction of nitryl chloride solutions was followed by a slow reaction which proceeded for many hours. With initial *p*-xylene and nitryl chloride concentrations 2·0M and 0·25M in nitromethane, the extent of chlorination after 1 hr. at −10° was 43%, after a further 2 hr. at 20° was 51%, and after a further hr. at 20° was 58%. Corresponding figures for mesitylene were 42, 52, and 66%. We concluded that the additional chlorination must be due to the other constituents present in yellow solutions, *viz.*, nitrosyl chloride and nitric acid. Measurement of the extent of chlorination by nitrosyl chloride, and nitrosyl chloride in the presence of nitric acid, confirmed this (Table 3).

TABLE 3. *Extent of chlorination of mesitylene* (0·1—1·0 *mole/l., in excess*) *by nitrosyl chloride at* 20°.

Reagent (Molar ratios)	Solvent	ArCl (%) (total) after 3 hr.	ArCl (%) (total) after 19 hr.	ArCl (%) (side-chain) after 5 hr.	ArCl (%) (side-chain) after 19 hr.
NOCl	$MeNO_2$	6	—	—	—
NOCl	MeCN	8	—	—	—
1·0 NOCl : 0·53 HNO_3	$MeCO_2H$	8	—	—	—
1·0 NOCl : 1·28 HNO_3	$MeNO_2$	15	—	—	—
1·0 NOCl : 2·0 HNO_3	$MeNO_2$	26	49	—	—
1·0 NOCl : 2·4 HNO_3	$MeNO_2$	—	—	6	7

(b) *Colourless solutions of nitryl chloride.* Nitryl chloride is unchanged when dissolved in benzene, methylene chloride, carbon tetrachloride, or ethyl acetate and when these solvents are used the nitryl chloride molecule or the chlorinium ion (Cl^+) derived from it is probably primarily responsible for the chlorination. That the extent of chlorination by such solutions is often considerably less than 100% can easily be explained as a result of the reaction of the nitrous acid, formed in the reaction, with unreacted nitryl chloride:

$$NO_2Cl + RH \longrightarrow RCl + HNO_2; \; NO_2Cl + HNO_2 \longrightarrow NOCl + HNO_3$$

Here again there is rapid chlorination followed by a slower one due to chlorination by nitrosyl chloride; for mesitylene in benzene the extent of chlorination at 20° after 1 hr., 3 hr., and 23 hr. is 61, 63, and 73% respectively, and the corresponding extents in ethyl acetate are 65, 65, and 71%.

The Kinetics of Chlorination.—The reaction of nitromethane solutions of nitryl chloride with the alkylbenzenes was too fast to follow even at −5°. The reaction was slowed down to a convenient rate by the use of 2 : 1 nitromethane–ether. A dilatometric method was employed, checked by a chemical one. The aromatic compound was always in excess (10-fold or more) to avoid the chlorination of the hydrocarbon being complicated by the further reaction of the chloro-aromatic product. The reaction was of first order with

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respect to the nitryl chloride (see Fig. 1). Unfortunately, the rate constants varied over a range of 25% and since we do not know why, the kinetics were of limited use. The lack of reproducibility might have been due to the catalytic effect of traces of water, but although elaborate precautions were taken to exclude moisture, subsequent results were no better.

Within the somewhat large experimental error, the first-order rate constant was independent of the initial nitryl chloride concentration; in 2 : 1 nitromethane–ether at −4·92° with an initial concentration of *p*-xylene 2·03M, k_1 for initial concentrations of nitryl chloride 0·07, 0·15, 0·17, 0·19, and 0·25 was 0·044, 0·060, 0·045, 0·052, and 0·053 respectively. However, the chemically determined rate constants were always slightly lower (*e.g.*, 0·044, 0·035, 0·035 min.$^{-1}$ in the same system at −5° and initial concentration of nitryl chloride 0·15M) than dilatometric ones (*e.g.*, 0·060, 0·045, 0·052 min.$^{-1}$). The reaction velocity was very dependent on the composition of the solvent; at −10° with

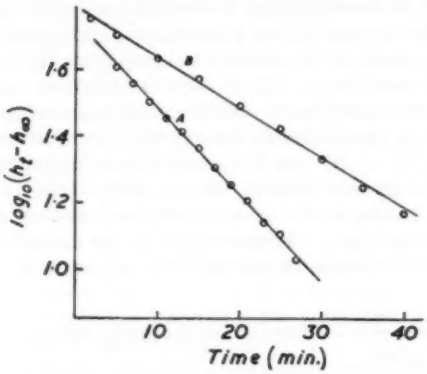


FIG. 1. *Rate of chlorination of* p-*xylene at* 5°.

A, Dilatometric, $k_1 = 0{\cdot}060$ min.$^{-1}$.
B, Chemical, $k_1 = 0{\cdot}035$ min.$^{-1}$.

initial concentration of *m*-xylene 2·0M, solvent ratios nitromethane : ether of 1 : 2, 3 : 10, and 1 : 10 gave k_1 0·10, 0·018, and 0·011 min.$^{-1}$ respectively. It varied with the aromatic compound; when the hydrocarbon was more reactive to electrophilic substitution than *p*-xylene, the reaction became too rapid to follow in 2 : 1 nitromethane–ether, and the proportion of ether had to be increased (Table 4).

TABLE 4. *Variations in* k_1 *with aromatic compound* (*initial concn. ca.* 2M).

Compound	Solvent $MeNO_2 : Et_2O$	Temp.	k_1 (min.$^{-1}$)
p-Xylene	2 : 1	−5°	0·050 (mean)
Toluene	2 : 1	−5	0·018 (mean)
m-Xylene	1 : 2	−10	0·10
,,	1 : 10	−10	0·011
Mesitylene	1 : 10	−10	0·088

An attempt was made to determine the order of reaction with respect to the aromatic compound by varying its initial concentration; the rate was unaffected, probably because the aromatic compound, being in excess, constitutes an appreciable fraction of the solvent. Thus an increase in rate caused by an increase in concentration of the aromatic compound might be compensated by a reduction in rate due to decrease in the polarity of the solvent.

All the results are consistent with a bimolecular attack on the aromatic compound by the chlorine molecule. Ultraviolet absorption spectra showed that nitryl chloride is hydrolysed similarly in nitromethane–ether as in pure nitromethane.

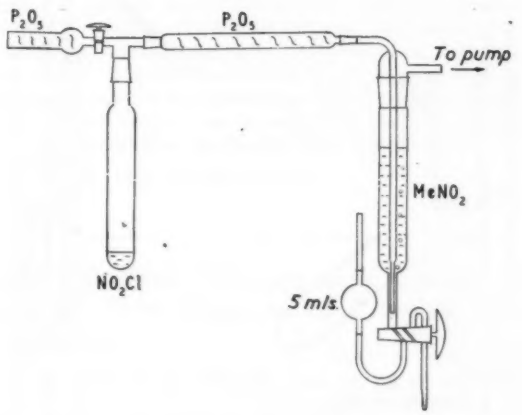
EXPERIMENTAL

Materials.—All compounds other than those in Part I were prepared and purified by standard methods.

Isolation of Reaction Products.—(a) *Nitryl chloride with excess of* p-*xylene. Separation of nitration product.* 150 ml. of *p*-xylene were added to 200 ml. of a 0·4M-nitryl chloride in nitromethane cooled to −10°. After 1 hr. the solution was allowed to warm to room temperature, and after a further hour was poured into water. The organic layer was separated, washed with water, and distilled at 15 mm. pressure. At 100° the distillation was stopped and the residue reduced with iron and hydrochloric acid. Last traces of *p*-xylene were extracted with ether. The aqueous layer was made alkaline and the amine product was ether-extracted. On evaporation of the ether a small residue of red oil was left which, acetylated with acetic anhydride, gave a product which, recrystallised from aqueous alcohol, had m. p. 137°, unchanged by admixture with 2-acetamido-*p*-xylene. The original reaction product therefore contained 2-nitro-*p*-xylene.

Separation of chlorination product. Another reaction mixture, obtained as above, was washed with water and evaporated at 100°/15 mm. The residue was dissolved in 100 ml. of light petroleum (b. p. 60—80°), filtered through a column of alumina, and eluted with light petroleum. The first portion of the eluate contained only traces of *p*-xylene. The next 200

FIG. 2.



ml. when evaporated left approximately 6 ml. of a colourless oil which distilled at 183° (b. p. of 2-chloro-*p*-xylene, 183°) (Found: C, 68·5; H, 6·70; Cl, 24·7. Calc. for C_8H_9Cl: C, 68·3; H, 6·45; Cl, 25·2%).

(b) p-*Xylene with excess of nitryl chloride.* A four-fold excess of nitryl chloride was used. The nitration and chlorination products were separated as above. The amine isolated was only sufficient to give an azo-dye test. The chloro-compound was large colourless plates, m. p. 70°, unchanged by admixture with 2 : 5-dichloro-*p*-xylene (Found: C, 54·5; H, 4·9; Cl, 39·4. Calc. for $C_8H_8Cl_2$: C, 54·9; H, 4·6; Cl, 40·5%).

(c) *Nitryl chloride with excess of mesitylene.* The method was similar to that for *p*-xylene. The amine was only sufficient for an azo-dye test. The chloro-compound was a colourless oil, b. p. 206° (b. p. of chloromesitylene, 204—206° (Found: C, 70·5; H, 7·31; Cl, 21·9. Calc. for $C_9H_{11}Cl$: C, 69·9; H, 7·12; Cl, 23·0%).

(d) *Mesitylene with excess of nitryl chloride.* 3 ml. of mesitylene were added to 200 ml. of *ca.* 0·5M-nitryl chloride in nitromethane. After 1 hr. the mixture was washed with water, then evaporated at low pressure to about 30 ml. On cooling, long white needles separated, m. p. 194°. Recrystallisation from alcohol to constant m. p. gave a product, m. p. 212° [2 : 4 : 6-trichloromesitylene prepared from chlorine and mesitylene had m. p. 209° (lit.,[4] m. p. 204—205°)] (Found: C, 47·6; H, 3·6; Cl, 47·6. Calc. for $C_9H_9Cl_3$: Cl, 48·2; H, 4·0; Cl, 47·7%).

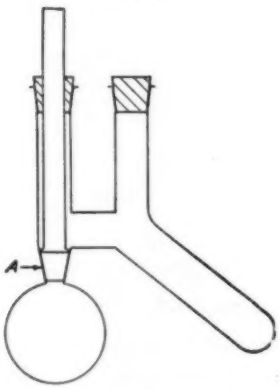
Determination of Reaction Products.—Aromatic nitro-compounds. When nitromethane was solvent, the method was similar to that of Bird and Ingold,[5] the nitromethane being extracted

[4] Fittig and Hoogewerff, *Annalen*, 1869, **150**, 328.
[5] Bird and Ingold, *J.*, 1938, 918.

with alkali and the residual aromatic nitro-compound titrated with titanous chloride. However, in order completely to remove the nitromethane without loss of the aromatic nitro-compound (which appeared to be soluble in an alkaline solution of nitromethane) we had to use a large volume of 5N-sodium hydroxide (200 c.c. per 5 ml. of sample) in place of the N-alkali used by them. The procedure employed for the titanous chloride reduction was based on that of Augood, Hey, and Williams.[6]

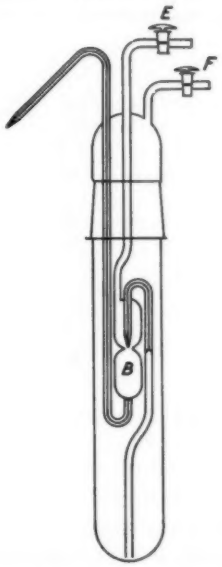
Organic chloro-compounds. Nitro-methane or -ethane was removed as above. With other solvents less vigorous treatment with alkali was required. The chloro-compound was then determined by a modification of Bacon's method.[7] *n*-Butanol was added to the aromatic residue and the mixture refluxed for 1½ hr. during the addition of metallic sodium. On cooling, diluting, and acidifying, the aqueous layer was separated and mixed with the washings of the butanol layer and the chloride present was titrated potentiometrically.

FIG. 3.



A, Ground stopper.

FIG. 4.



In some cases the extent of chlorination was estimated more simply from the reduction during the reaction of the hydrolysable chloride in the reaction mixture. Side-chain chlorination products were determined by the same method except that the aromatic residue was refluxed with sodium butoxide instead of metallic sodium.

Reaction Kinetics.—Dilatometry. A solution of nitryl chloride was prepared by distilling the oxyhalide over phosphoric oxide into nitromethane by using the apparatus shown in Fig. 2. The kinetic runs were carried out in groups of four. 5 ml. of the nitryl chloride solution were pipetted into the bulb of each mixing flask (Fig. 3), and a sample was analysed. 5 ml. of a solution of the aromatic compound in ether were placed in the other arm of each flask. One flask was placed in the thermostat and the others were cooled in solid carbon dioxide. After temperature equilibrium had been obtained, the bulb of the mixing flask was unstoppered by withdrawing the rod through the greased Polythene stopper. The solutions were mixed by tilting the flask, the stopper was withdrawn and a tapless dilatometer (Benford and Ingold [8] type *C*) filled.

Chemical determination of reaction velocities. A solution of nitryl chloride in nitromethane was placed in the tube of the apparatus illustrated in Fig. 4, and immersed in the thermostat

[6] Augood, Hey, and Williams, *J.*, 1952, 2097.
[7] Bacon, *J. Amer. Chem. Soc.*, 1909, **31**, 49.
[8] Benford and Ingold, *J.*, 1938, 929.

up to the ground joint. An equal volume of an ether solution of the aromatic hydrocarbon at the thermostat temperature was then rapidly added. Samples were withdrawn at intervals and hydrolysed, and the liberated chloride titrated with silver nitrate. The samples were withdrawn without exposure to the atmosphere as follows. The mixture was blown into the bulb *B* (capacity 2·45 ml.) by blowing dry air into *F* with tap *E* open. When the bulb was full, the pressure at *F* was released, and the excess of the solution in the upper bulb syphoned back into the bulk of the reaction mixture. By closing *F* and blowing dry air through *E*, the liquid in the bulb *B* was forced out through the capillary tube and collected in a flask containing a little water.

Check of the stability of chlorine and nitryl chloride in nitromethane and ether solvents. When it was realised that free chlorine was present in solutions of nitryl chloride in nitromethane the stability of solutions of chlorine was investigated. Solutions of chlorine (*ca.* 0·05M) were stable in pure nitromethane at −5°, but in pure ether they slowly reacted, losing 15% of oxidising power in 3 hr. although there was no loss of ionisable chlorine. Solutions in 2 : 1 nitromethane–ether were, surprisingly, much less stable, losing 70% of oxidising power in 1 hr.

When the stability of nitryl chloride in nitromethane and ether was originally investigated the total acid and chloride produced on hydrolysis were determined and there was no change with time. In view of the reaction of free chlorine, the reducing power of nitryl chloride solutions was determined. A solution of nitryl chloride in pure nitromethane was stable, that in ether very slowly developed reducing action at −5°, but again with the mixed solvent the development was more rapid. The rise in reducing power of the solution during 40 min. at −5° was equivalent to the removal of the oxidising power of one third of the chlorine originally present. Since most kinetic runs were over in under 30 min. the reaction with the solvent clearly would not invalidate the general conclusions from the kinetics.

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80. *The Interaction of Metal Chlorides with Organic Chlorides. Part I. Freezing-point Phase Diagrams of Titanium Tetrachloride with Some Alkyl Chlorides.*

By W. R. LONGWORTH, P. H. PLESCH, and (in part) (the late) M. RIGBI.

The freezing-point phase diagrams of titanium tetrachloride with each of six alkyl chlorides were determined by using a greaseless high-vacuum system. With methyl chloride, methylene dichloride, and chloroform titanium tetrachloride forms simple eutectic systems. With ethyl chloride, *iso*propyl chloride, and ethylidene dichloride the phase diagrams show discontinuities; these are not due to the formation of complexes in solution. When mixtures of titanium tetrachloride and alkyl chlorides are exposed to direct daylight one product is titanium trichloride.

INVESTIGATIONS on the mechanism of cationic polymerisations indicated the need for information on the interaction of titanium tetrachloride with alkyl chlorides. Only two such studies have been reported. Nasu [1] determined the freezing-point phase diagram for titanium tetrachloride and carbon tetrachloride and found a pure eutectic system. Butta [2] investigated the liquid–vapour equilibrium of mixtures of titanium tetrachloride and *s*-tetrachloroethane, and reported no interaction. We wanted to find out whether titanium tetrachloride reacts with alkyl chlorides, because several alkyl chlorides co-catalyse the polymerisation of olefins by metal halides and the reaction $RCl + MCl_n \longrightarrow R^+MCl_{n+1}^-$, originally suggested by Pepper [3] for the system ethylene dichloride–stannic chloride, has so far not been substantiated directly. We chose to determine the freezing-point phase diagrams of the binary systems, as the technique is

[1] Nasu, *Bull. Chem. Soc. Japan*, 1933, **8**, 195.
[2] Butta, *Chem. Listy*, 1956, **50**, 1646.
[3] Pepper, *Trans. Faraday Soc.*, 1949, **45**, 397.

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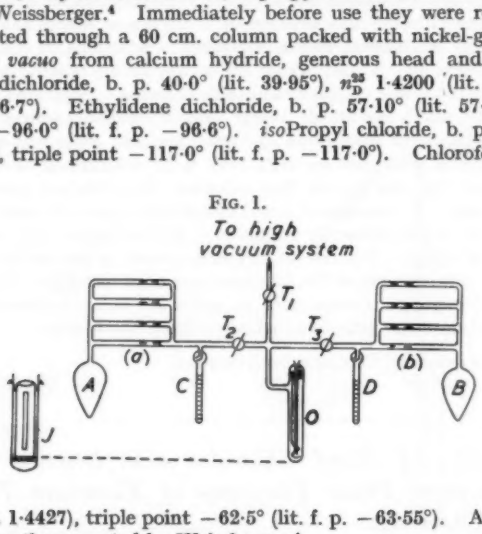
relatively simple, the results fundamentally unambiguous, and the information obtained related to the temperature range of most interest for cationic polymerisations.

Experimental

Materials.—Titanium tetrachloride (British Titan Products Ltd.) was filtered, twice fractionated, and sealed into phials; b. p. 134°/735 mm. Immediately before use the material was thrice fractionated *in vacuo*; triple point −23·9° (lit. −24·2°).

Methylene dichloride, ethylidene dichloride, *iso*propyl chloride, and chloroform were purified as recommended by Weissberger.[4] Immediately before use they were refluxed over calcium hydride and fractionated through a 60 cm. column packed with nickel-gauze rings, and then twice fractionated *in vacuo* from calcium hydride, generous head and tail fractions being rejected. Methylene dichloride, b. p. 40·0° (lit. 39·95°), n_D^{25} 1·4200 (lit. 1·4201), triple point −95·0° (lit. f. p. −96·7°). Ethylidene dichloride, b. p. 57·10° (lit. 57·31°), n_D^{25} 1·4146 (lit. 1·4145), triple point −96·0° (lit. f. p. −96·6°). *iso*Propyl chloride, b. p. 34·94° (lit. 34·80°), n_D^{25} 1·3753 (lit. 1·3755), triple point −117·0° (lit. f. p. −117·0°). Chloroform, b. p. 61·00° (lit. 61·00°), n_D^{25} 1·4431 (lit. 1·4427), triple point −62·5° (lit. f. p. −63·55°). All b. p.s are corrected. All literature values are those quoted by Weissberger.[4]

Fig. 1.



Ethyl chloride gas (I.C.I.) was passed through towers containing soda-lime, calcium chloride, and phosphoric oxide and condensed into a flask containing calcium hydride and twice fractionated *in vacuo*, generous head and tail fractions being rejected; triple point −133·4° (lit. f. p. −136·4°).

Methyl chloride gas (I.C.I.) was passed through towers containing aluminium chloride, soda-lime, and phosphoric oxide, thrice fractionated *in vacuo*, generous head and tail fractions being rejected at each stage, and stored as a gas; triple point −95·1° (lit. f. p. −97·72°).

Thermal Analysis.—Apparatus. The apparatus for the thermal analysis had to satisfy stringent conditions: (*a*) Freedom from adventitious moisture. (*b*) Complete absence of organic materials such as tap grease and of mercury, as these are attacked by titanium tetrachloride.

The apparatus is shown in Fig. 1. An observation vessel, *O*, contained a central thermocouple pocket and a reciprocating stirrer, operated by a solenoid (not shown). To obtain slow and uniform cooling, two concentric tubular jackets *J* of copper (inner) and Pyrex glass (outer) were fitted round the observation vessel during the determination of the cooling curves. The pure components were stored in the reservoirs *A* and *B* from which the burettes *C* and *D* could be filled *via* the magnetic " breakseals " (*a*) and (*b*). The all-metal valves T_1, T_2, and T_3 have been described.[5] The 5-point copper–constantan thermocouple, with the constant-temperature junctions in melting ice, was calibrated by the freezing points of carefully purified carbon tetrachloride, mercury, chloroform, and toluene.

In the earlier experiments the E.M.F. of the thermocouple was measured at half-minute intervals on a " Doran Mini " potentiometer. For later experiments a recording potentiometer

[4] Weissberger, " Techniques of Organic Chemistry, Vol. VII—Organic Solvents," Interscience, London, 1955.

[5] Biddulph and Plesch, *Chem. and Ind.*, 1956, 569.

was constructed to record the E.M.F. continuously on a moving chart, *i.e.*, it drew the cooling curves automatically.

Operation.—The two components were distilled into the observation vessel from the burettes, which were kept in a thermostat of melting ice, by cooling it in liquid air. Before determining the cooling curves of the mixtures, those of the pure materials were always determined. When the required mixture had been made up in the observation vessel, it was allowed to melt, the stirrer was started, the cooling jackets placed in position, and the whole assembly then immersed in liquid air; the level of this was so adjusted that a cooling rate of 7—10° per min. was obtained. The recording of the E.M.F. of the thermocouple was started simultaneously and continued down to or below the eutectic temperature of the mixture. Many cooling curves were repeated two or more times and, in the later experiments particularly, warming curves were also obtained. After a satisfactory cooling curve had been obtained, a small portion of one component was distilled into the observation vessel. The cooling curve was then obtained as before. The procedure was repeated until the observation vessel became too full for satisfactory agitation (approx. 10 ml.). The contents were then either pumped off or distilled into special phials for further observation. The whole procedure was repeated, starting from the opposite end of the composition range. Finally, a third and sometimes a fourth series of measurements was undertaken.

Errors.—Temperature of inflection. The E.M.F. of the thermocouple could be read to an accuracy of 0·02 mv, which corresponds to 0·12°. The inflection points on the cooling curves could be located with an accuracy of ±0·5° in the most difficult cases.

Composition. The error in the composition is essentially determined by the precision with which the volumes can be measured and is greatest at the ends of the composition range. To measure this error, four samples of 0·2 ml. of methylene dichloride were distilled into weighed phials by a procedure identical with that used in the runs. From the results we calculated that the uncertainty in composition varies from 8% of the proportion of the scarcer component at the ends, to 0·3% at the centre of the composition range.

Vapour-pressure measurements. The vapour-pressure measurements were not intended to be very accurate, being rather to obtain the general shapes of the vapour pressure–temperature curves for mixtures of methylene dichloride and titanium tetrachloride in order to see whether they showed any inflections. Accordingly, an ordinary mercury manometer was connected to the observation vessel through an all-metal tap. The vapour-pressure measurements were made during the recording of the cooling curves by the automatic recorder, and the time of reading marked on the chart electrically. Thus, the pressure readings could be correlated with the appropriate temperatures. The vapour-pressure curve of pure methylene dichloride so obtained agreed satisfactorily with that in the literature. No interference by mercury vapour was observed: possibly it amalgamated with the metal tap.

Results

Thermal Analysis.—The interpretation of many of the cooling curves, mainly those of the type *A* in Fig. 2, was unambiguous. For many other curves it was less clear, as their shapes differed from the " ideal " shapes; typical examples are curves *B*, *C*, *D*, and *E* (Fig. 2). For curves of these types, the points marked (*a*) were chosen as giving a better indication of the first inflection than those marked (*b*), although expert opinion on this is not unanimous. The eutectic arrests were usually of the type shown at (*t*) in curves *A*, *B*, *D*, and *E* (Fig. 2). In certain cases, usually at the end of the phase diagram distant from the eutectic composition, they were of the type shown at (*d*) in curve *C* (Fig. 2), with a straight sloping branch in place of the true flat. The eutectic temperature was reasonably constant near the eutectic composition but tended to drift as the composition moved away from this.

With methylene dichloride, ethyl chloride, methyl chloride, and *iso*propyl chloride, a hump, shown at (*f*) in curve *B* (Fig. 2), was found after the first inflection point, which was normal, and before the eutectic, which was also quite normal. This phenomenon appeared only in the region of the phase diagram below the steeply falling portion of the liquidus curve. In this region very little solid is deposited for a given fall in temperature, so it is notoriously difficult to obtain accurate liquidus points by total thermal analysis. The inflection (*a*) is the true liquidus point and the hump (*f*), due to delayed precipitation, can be ignored.[6]

[6] Axon (Metallurgy Dept., The University, Manchester), personal communication.

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In several curves additional inflection points occurred such as those shown at α and β on curve *E* (Fig. 2). The change in slope was always small and, in view of the well-defined first inflection point (*a*), the equally well-defined eutectic (*t*), and the fact that these points did not occur in the warming curves, they were regarded as spurious.

FIG. 2.

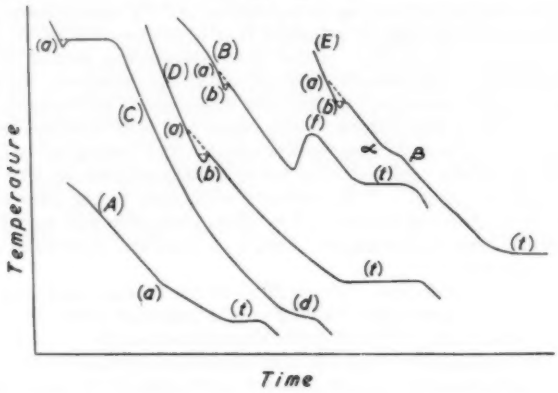
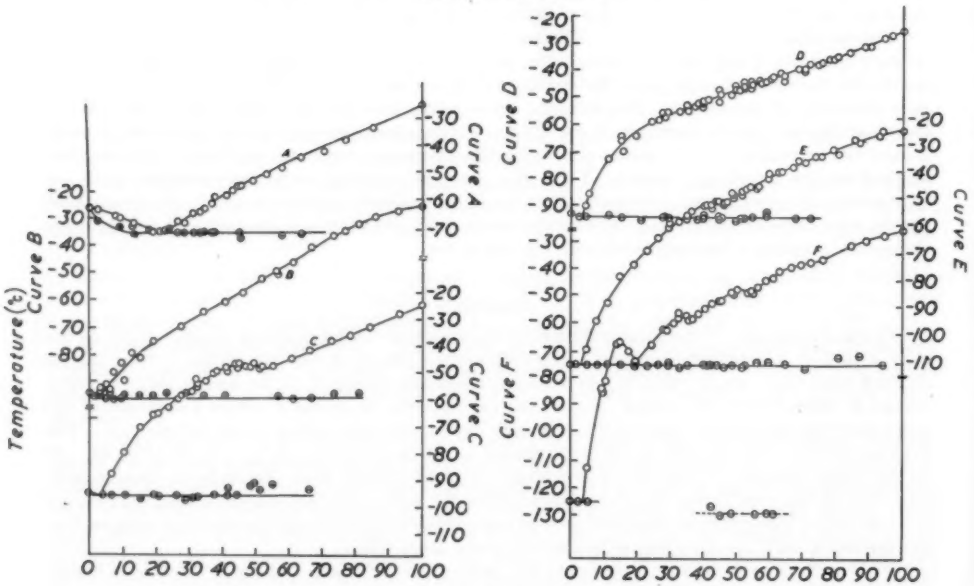


FIG. 3. *Phase diagrams of systems of* $TiCl_4$ *with A,* $CHCl_3$; *B,* MeCl; *C,* $Me{\cdot}CHCl_2$; *D,* CH_2Cl_2; *E,* Me_2CHCl; *F,* EtCl.



The presence of a liquidus point and a eutectic point in all the phase diagrams, with the exception of the left-hand branch of the chloroform–titanium tetrachloride diagram, rules out the possibility of solid solutions over a wide range of the phase diagrams; but near the extremities, solid solutions might have escaped detection.

Qualitative Observations.—The colour and appearance of the material were noted at the end of each cooling curve, and in some cases the cooling curve was interrupted to observe the solid formed at the first transition point. This always consisted of colourless plate-like crystals. In four of the six systems, yellow colorations were observed at the lower temperatures. This colour, when formed, was discharged on warming, and reappeared on cooling. The liquid phase was always colourless. With methylene dichloride, a thin yellow layer appeared at the top of an otherwise colourless solid mass at the eutectic temperature (−96·1°) in mixtures containing 5·43, 28·35, 52·10, 55·50, and 76·80 moles % of methylene dichloride severally. All other mixtures were colourless even below the eutectic temperature.

With ethyl chloride, a yellow colour appeared at approximately −105°, *i.e.*, above the eutectic temperature. This also disappeared as the temperature was raised and was found in mixtures containing 11·45, 33·99, 39·29, 41·58, 43·70, and 57·59 moles % of ethyl chloride. The mixture containing 72·00 moles % of ethyl chloride had a yellow layer on top of the solid mass at the eutectic temperature (−138·00°), and the mixture containing 34·88 moles % of ethyl chloride was yellow throughout at this temperature.

FIG. 4.

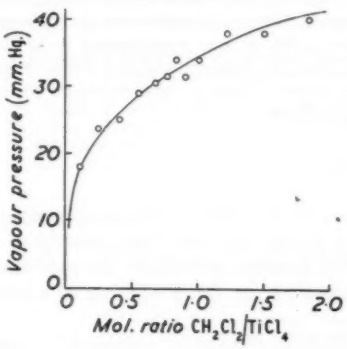
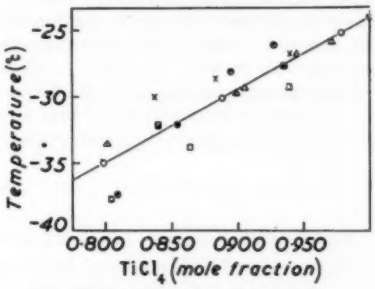


FIG. 5. *Solubilities.*



○ Ideal solubility of $TiCl_4$.

Solubility of $TiCl_4$, taken from the phase diagrams, in ● $CHCl_3$, ◓ MeCl, ◒ Me·$CHCl_2$, △ CH_2Cl_2, □ Me_2CHCl, × EtCl.

In the *iso*propyl chloride system, the yellow colour appeared at approximately −85° to −92° and was discharged on further cooling, the mixture being colourless at the eutectic temperature; the colour reappeared on warming to approximately −90°. This colour was noted in 26 runs, the composition varying from 6·20 to 97·80 moles % of *iso*propyl chloride.

With methyl chloride, the solid at the eutectic temperature was coloured throughout with mixtures containing more than 33·35 moles % of methyl chloride. Below this concentration, no colour was observed.

No colour changes were observed in the systems chloroform– and ethylidene dichloride–titanium tetrachloride.

Effect of Light.—When mixtures of titanium tetrachloride and various alkyl chlorides, sealed *in vacuo* into phials, were exposed to direct daylight a deposit was formed whose colour varied from bright purple to brown; this was due to lower chlorides of titanium, probably mostly the trichloride. We therefore kept all the pure components and the mixtures used for the thermal analyses in subdued light. The photochemical reaction is being investigated. Puxeddu [7] found that mixtures of various metal chlorides, including titanium tetrachloride, with diethyl ether yielded lower chlorides in sunlight.

Phase Diagrams.—The results obtained by thermal analysis of titanium tetrachloride–methylene dichloride, –chloroform, –ethylidene dichloride, –*iso*propyl chloride, and –methyl chloride are represented in the phase diagrams (Fig. 3) which show the following features (all records of moles % relate to the organic chloride).

[7] Puxeddu, *Gazzetta*, 1929, **59**, 160.

(a) *Chloroform.* A simple eutectic system with solid solution formation on the chloroform-rich side of the eutectic composition. Eutectic temperature −71·4° and eutectic composition approximately 81·0 moles %.

(b) *Methyl chloride.* A simple eutectic system with eutectic temperature −97·0° and eutectic composition between 98·0 and 100 moles %.

(c) *Ethylidene dichloride.* In this diagram there is a flat hump with a peak near −45·7° and composition 55·0 moles %. There is a single eutectic at −97·25° and 96·0 moles %.

(d) *Methylene dichloride.* A simple eutectic system with the eutectic temperature −96·1° and the eutectic composition approx. 97·6 moles %.

(e) iso*Propyl chloride.* There is a flat hump with a peak near −64·5° and composition 44·0 moles %. The temperature of the single eutectic is −117·0° and the composition 98 moles %.

(f) *Ethyl chloride.* This diagram shows one pronounced peak and three smaller ones; the peak temperatures are −66·0°, −56·3°, −46·5°, and −36·3°, respectively, and the corresponding compositions 85·0, 65·6, 50·0, and 29·0 moles %.

Vapour-pressure Measurements on the System Titanium Tetrachloride–Methylene Dichloride.—The pressure–temperature curves had two inflection points, corresponding to the deposition of a solid phase and of the eutectic solid. In most cases the points of inflection were easily seen but in some, especially at the methylene dichloride-rich end of the phase diagram, they were very obscure. The liquidus curve and the eutectic line defined by these inflection points were identical with those of Fig. 3(*D*). An isotherm at −29·0° (Fig. 4) was constructed from the *P*–*T* curves covering the range 0—2 molar ratio $[CH_2Cl_2]/[TiCl_4]$; beyond this the points were too scattered to be significant. Fig. 4 shows that in this system there is no compound formation and thus supports the conclusions from the thermal analysis.

Discussion

These phase diagrams are condensed phase diagrams as the effect of changing pressure has been ignored. Their interpretation is complicated by the fact that the presence of a hump or peak in a melting-point phase diagram does not necessarily indicate the existence of a compound in solution; such discontinuities may arise from the formation of superlattices.

The phase diagrams for titanium tetrachloride–methylene dichloride, –chloroform, and –methyl chloride are those of simple eutectic systems and show no evidence of interaction.

The systems titanium tetrachloride–ethylidene dichloride and –*iso*propyl chloride show a discontinuity in the liquidus curve. However, the occurrence in each diagram of a single eutectic covering the greater part of the concentration range, and the absence, in both systems, of a second eutectic at the temperature of the discontinuity, make it extremely unlikely that the discontinuities are due to compound formation in solution.

The phase diagram of the system titanium tetrachloride–ethyl chloride is completely different. In spite of its peculiar character, we present it with some confidence because it agrees very closely with earlier unpublished results obtained here by a similar but more primitive technique.[8] Although the peaks correspond closely to $[C_2H_5Cl]/[TiCl_4]$ ratios of 6 : 1, 2 : 1, 1 : 1, and 1 : 3, we do not consider that they can be attributed to the existence of compounds in solution because a very careful search failed to reveal any trace of the corresponding eutectics. Moreover, the eutectic in the vicinity of −133° occurs also in the central region of the phase diagram.

The ideal solubility of titanium tetrachloride can be calculated from the formula:

$$\log X_A = (-L_f/2{\cdot}303R)(1/T_0 - 1/T)$$

where X_A is the mole-fraction of titanium tetrachloride, by using $T_0 = 249{\cdot}1°$ K and $L_f = 2371{\cdot}6$ cal./mole.[9] This is shown in Fig. 5, together with the actual solubilities of titanium tetrachloride in the various alkyl chlorides taken from the phase diagrams.

[8] Plesch and Rigbi, unpublished results.
[9] Clabaugh, Leslie, and Gilchrist, *J. Res. Nat. Bur. Stand.*, 1955, **55**, No. 5.

These points all lie very close to the ideal solubility curve, and this apparently nearly ideal behaviour over a considerable concentration range also suggests that there is no strong interaction in solution between titanium tetrachloride and these alkyl chlorides.

It thus appears that the ionogenic reaction suggested by Pepper [3] occurs either not at all or only so very slightly that its detection may require more subtle methods. Even without detailed analysis,[10] it is evident that the energetics of the ionisation are governed by the heterolytic bond-dissociation energy (θ) of the organic chloride.[11] The fact that the ionisation is not readily detectable in the systems investigated here, but is quite easily demonstrable in systems involving triarylmethyl halides,[12,13] is undoubtedly primarily due to the fact that for triphenylmethyl chloride θ is of the order of 125 kcal./mole, whereas for our chlorides it ranges from 165 kcal./mole for *iso*propyl chloride to 230 kcal./mole for methyl chloride. A preliminary investigation of the system titanium tetrachloride–*tert.*-butyl chloride ($\theta = 147$ kcal./mole) revealed a complex behaviour which may indicate ionisation. This work is continuing.

We acknowledge a Research Assistantship by the D.S.I.R. (to M. R.), funds from Esso Research Limited (to W. R. L.) and the Chemical Society's Research Fund, and a gift of especially pure titanium tetrachloride from Messrs. British Titan Products Limited. We also thank Dr. R. H. Biddulph and Dr. H. J. Axon (Manchester University) for help and advice.

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KEELE, STAFFORDSHIRE. [*Received, June 7th*, 1957.]

[10] Plesch, *Z. Elektrochem.*, 1956, **60**, 325.
[11] *Idem*, "Simposio Internazionale di Chimica Macromoleculare," *Ricerca sci.*, 1955, 140.
[12] Fairbrother and Wright, *J.*, 1949, 1058.
[13] A. G. Evans *et al.*, *Research*, 1952, **5**, 535; *J.*, 1955, 206; 1955, 3104; 1957, 1020.

81. *A Possible Differentiation between Ion-pairs and Complexes.*

By J. M. SMITHSON and R. J. P. WILLIAMS.

A study has been made of the association between several anions and the cobaltous ion. The absorption spectra of the species involved are discussed as they lead to a possible method for distinguishing between transition-metal cation complexes and ion-pairs.

Ion-pairs and Complex Formation.—A simple theoretical distinction between the complex of a cation M and a ligand L and an ion-pair can be made by looking upon the former as the associated group ML in which L is adjacent to M and the latter as an associated unit M(S)L where S, a solvent molecule such as water, lies between M and L.* The distinction has been of limited use because most methods of examination of a solution containing M and L will not distinguish between the alternatives. However if M is a transition-metal cation, such as cupric, and has two sets of absorption bands, one of high intensity in the ultraviolet and one of much lower intensity in the visible region, as is generally so for such cations, a possible method of differentiation arises. The weak bands in the visible region are forbidden *d*–*d* transitions and the wavelength of the absorption depends on the separation (splitting) of the *d* states. This splitting is a function of the polarisation of the cation by the ligand. The splitting therefore depends upon a high power of the inverse of the distance of separation, r, between the ligand and the cation, possibly varying [1] as r^{-5}. Ion-pair formation will be expected then to have very little effect on this *d*–*d* splitting because of the large separation between M and L in ion-pairs. The ultraviolet bands of the solutions of transition-metal cations are considered to be

* It is not an essential part of this definition that there should be only one solvent molecule between M and L but that there should be at least one.

[1] Jørgensen, *Acta Chem. Scand.*, 1955, **9**, 405.

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charge-transfer bands.[2] The dependence of the stability of the excited state relative to the ground state upon r therefore must be more nearly as r^{-1} than r^{-5} as the expression for the energy of interaction in one (or both) of the states contains [2] terms in r^{-1}. Both ion-pair and complex formation will be expected to affect the position of the ultraviolet bands, the latter to the greater degree. Naturally changes of extinction coefficient are expected concomitant with changes in the position of the absorption but it has not been possible to develop a generally accepted theoretical discussion.[1,3]

Thus, by observing changes in both ultraviolet and visible spectra in a series of transition-metal complexes we might be able to discover whether ion-pairs or complexes were formed. This examination will be the more thorough if it is made together with studies of activity coefficients. The method of treating association equilibria should be capable of extension to studies of anions in which there are forbidden transitions, *e.g.*, the nitrate ion, for all such transitions depend upon changes in polarisation of one member of the unit ML rather than on changes in the dipole of ML.

As examples we will consider some cobaltic complexes and ion pairs, where the differentiation between the two types of association can be made clearly as the rate of exchange of ligands in the co-ordination sphere is extremely slow. Table 1 lists [4] some

TABLE 1. *Absorption spectra of pentamminocobaltic complexes.*

Ligand in 6th co-ordination place ...	NH_3	H_2O	SCN^-	$S_2O_3^{2-}$	NO_3^-	SO_4^{2-}	Cl
$\lambda_{max.}$	472	490	497	500	500	515	531
log $\epsilon_{max.}$	1·74	1·68	2·28	—	1·75	1·75	1·71

spectroscopic observations on pentamminocobaltic complexes in which there is one further ligand. In these associated units the anion is adjacent to the cation. The absorption band referred to in the Table is due to an internal *d–d* transition of the cobaltic ion and is sensitive to the ligand in the complex as expected.

In two or three cases the corresponding hexamminocobaltic and aquopentamminocobaltic ion pairs have also been studied, in which it is known from exchange studies that the anion and cation are not adjacent. For example Taube and Posey [5] found that the position and the intensity of the absorption band due to the *d–d* transition of the aquopentamminocobaltic sulphate ion-pair were the same as those of the unassociated perchlorate. Similar observations [6] have been made on the chloride, bromide, and iodide ion-pairs of this cation and of the hexamminochromic cation. Although there are no changes in the *d–d* bands, the ultraviolet absorption spectra, of high extinction, is considerably modified. Bale, Davies, and Monk have shown [7] that on the formation of the hexamminocobaltic sulphate and thiosulphate ion-pairs there is no change in the visible absorption although the ultraviolet absorption changes appreciably. In all these cases the stability of the ion-pairs could be calculated from the changes in the ultraviolet spectra with concentration of the ions. Such observations are in keeping with the theoretical argument made above. In the study [5] of the association of sulphate and the aquopentamminocobaltic ion it was shown that the equilibrium constants for the formation of the ion-pair $[Co(NH_3)_5H_2O]^{3+}SO_4^{2-}$ and for the complex $[Co(NH_3)_5SO_4]^-$ were almost equal. We will show that what we take to be the ion-pair of cobaltous sulphate has almost the same stability as the complex of cobaltous thiosulphate.

The nitrate ion has a forbidden transition which gives rise to absorption around 300 mμ. In organic solvents spectra of solutions of anhydrous nitrates show that this band is considerably modified and it has been generally accepted that the change is brought about

[2] Orgel, *Quart. Rev.*, 1954, **8**, pp. 424 and 440.
[3] Ballhausen, *Acta Chem. Scand.*, 1955, **9**, 821.
[4] von Kiss and Czegledy, *Z. anorg. Chem.*, 1938, **235**, 407.
[5] Taube and Posey, *J. Amer. Chem. Soc.*, 1953, **75**, 1463.
[6] Linhard and Weigel, *Z. anorg. Chem.*, 1951, **266**, 49.
[7] Bale, Davies, and Monk, *Trans. Faraday Soc.*, 1956, **52**, 816.

by the polarisation of the nitrate anion in complexes with the cations.[8] Supporting this deduction is the fact that the greatest changes in the nitrate band occur in the order of cations of transition metals, A-sub-group metals of high charge or small size, A-sub-group metals of low charge or large radius (*e.g.*, $Li^+ > K^+$, $Mg^{2+} > Ca^{2+}$). In aqueous solutions of the same molarity the order of the effect of different cations is completely altered to $K^+ > Li^+$ and $Ba^{2+} > Ca^{2+} > Mg^{2+}$,[9,10] which suggests that the larger cations form complexes to the greater degree. The study of activity coefficients of nitrates has been taken to show that it is the larger cations which associate with the nitrate ion to the greater extent.[11] In the case of lead nitrate[12] the two methods, studies of absorption spectra changes and of reversible electrode potentials, led to the same association constant. As the spectroscopic method depended on examining the intensity changes of a forbidden transition we consider that a complex is formed. Now if the perchlorates of bivalent cations are taken as a standard of non-associated 1 : 2 electrolytes then the activity coefficients of all nitrates, which are lower, imply some kind of specific interaction. By examining the spectra of solutions of a transition-metal nitrate both in the region of the nitrate absorption and that of the cation absorption, complex formation should be easily detected. Moreover apart from the perchlorate we can use the chloride ion and the iodide ion as reference anions as the activity coefficients of many iodides are very like those of perchlorates and the activities of certain chlorides are very like those of nitrates, *e.g.*, cobaltous. We have chosen the cobaltous cation for this study as the absorption spectra of cobaltous salts are very sensitive, especially in intensity, to changes in the co-ordinating ligands.

Experimental

We studied the changes in absorption spectra of cobaltous ion solutions in media of constant ionic strength. The conditions are given in Table 2. Univalent perchlorates were used to make up the ionic strength.

The measurements were made with the Unicam S.P. 500 and 600 spectrophotometers with matched cells at 20° ± 1°. All absorption spectra were measured against blanks made up in the same manner as the test solution but with the cation omitted. All reagents were " AnalaR." As all previous spectrophotometric measurements on these systems[13–15] were made without a constant ionic-strength background and without appropriate blanks we cannot strictly compare them with our observations nor is it easy to use them to discuss the spectra or stability of individual complexes ML.

Results.—We will take the study of the thiocyanate solutions as a typical example. Two changes in the absorption bands appear on adding thiocyanate to cobaltous perchlorate. One is at 275 mμ where the absorption is of high extinction. This is considered to be a charge-transfer band. The second is a smaller change, being a modification of the *d–d* transition, at 575 mμ. The two bands increase proportionately, showing that they belong to species which have the same dependence on thiocyanate concentration. The simplest assumption satisfying this condition is that they belong to the same species, which we take to be an associated unit Co/CNS, leaving it to be decided whether it is a complex or an ion-pair. Making this simplest assumption and observing that neither thiocyanate ions nor cobaltous perchlorate absorbs appreciably at 275 mμ, we derive the following expression

$$K = E_m \,.\, Co_T/\{E_x[Co_T - (E_m \,.\, Co_T/E_x)][T_x - (E_m \,.\, Co_T/E_x)]\} \quad . \quad . \quad . \quad (1)$$

where Co_T is the total cobalt concentration, E_x the (unknown) extinction coefficient of CoSCN for the given Co_T, E_m the measured extinction per mole of cobalt (which varies with

[8] Katzin, *J. Chem. Phys.*, 1950, **18**, 789.
[9] Halban, *Z. Electrochem.*, 1928, **34**, 489.
[10] Kortum, *ibid.*, 1944, **50**, 144.
[11] Williams, *J.*, 1952, 3770.
[12] Hershenon, Smith, and Hume, *J. Amer. Chem. Soc.*, 1953, **75**, 507.
[13] von Kiss and Csokan, *Z. phys. Chem.*, 1940, **186**, *A*, 289
[14] von Kiss and Major, *ibid.*, 1941, **189**, *A*, 364.
[15] von Kiss and Gerendas, *ibid.*, 1937, **180**, *A*, 117.

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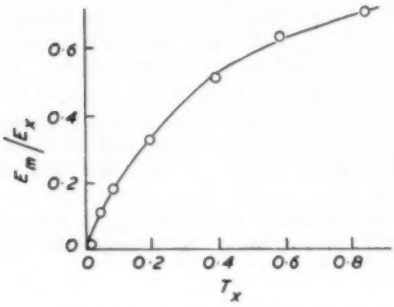
T_x, the total thiocyanate concentration), and K is the desired equilibrium constant [CoSCN]/([Co][SCN]) for the given ionic strength.

When $T_x \gg Co_T$, a plot of $1/T_x$ against $1/E_m$ is linear with intercept $-K$ and slope KE_x. Using the values of K and E_x so derived we can test eqn. (1) over the whole range of T_x values; it is obeyed (see Figure). The equations are equally valid with data at a different wavelength. The same equations have been applied to the other systems giving the results in Table 3. The ionic strengths are given earlier, and the conditions in Table 2.

The fact that the equations hold so well supports the assumption that there is only one associated species within the range of the measurement, *i.e.*, Co/SCN in the case of the thiocyanate. The formation constant of the thiosulphate K can be compared with that obtained ($1{\cdot}2 \times 10^3$) by Denney and Monk [16] using a conductivity method. Ours, found by a very



Plot of total thiocyanate concentration (M) *against the degree of formation of the thiocyanate complex.*

Full line from eqn. (1), and experimental points by use of data in Table 3. Total cobalt concentration 0·05M.

lengthy extrapolation by the Davies equation,[17, 18] is 5×10^1. The agreement is as good as can be expected, the known limitations of the extrapolation being considered, and is very similar to that found when comparing studies by optical and other methods on the association of cupric sulphate.[19] † A modified procedure was adopted in the treatment of the chloride data

TABLE 2. *Conditions used in the study of cobaltous complexes.*

Ligand	Cl^-	SCN^-	$S_2O_3^{2-}$	SO_4^{2-}	I^-	NO_3^-
Concn. (ligand molarity)...	0·40—2·15	0·05—0·85	0·01—0·25	0·01—0·25	0·80—7·00	0·05—0·85
Ionic strength (M)	7·0	1·0	1·0	1·0	7·0	1·0

TABLE 3. *Association constants and absorption spectra of some cobaltous complexes.*

Ligand	K	Species	$\lambda_{max.}$ (mμ)	$\varepsilon_{max.}$	$\lambda_{max.}$ (mμ)	$\varepsilon_{max.}$
ClO_4^-	—		No measurable association of any kind			
SCN^-	2·5	$CoCNS^+$	275	1140	516	44·4
Cl^-	0·37	$CoCl^+$	250	—	529	12·7
$S_2O_3^{2-}$	2·35	CoS_2O_3	295	620	512	375
SO_4^{2-}	?	$CoSO_4$ *	No observable change in visible			
NO_3^-	?	$CoNO_3^+$ *	No observable change in visible			
I^-	—		No measurable association of any kind			
H_2O	—	—	<250	—	512	4·75

* Species presumed present from activity coefficient changes (see text).

for the formation of a second complex, $CoCl_4^{2-}$, interferes. Allowance was readily made for this complex, however, as its absorption bands are much more intense and at considerably longer wavelength. Our method was to determine the absorption spectrum of the fully formed $CoCl_4^{2-}$, in the presence of 10M-lithium chloride, and then to use the value of the extinction coefficient so found to determine the amount of cobalt bound as $CoCl_4^{2-}$ at any chloride concentration. The calculation then proceeded as above and the fact that the equilibrium

† The association constant for cupric sulphate at ionic strength 1·0 is 4·0 and by ionic-exchange methods 9·0. The association constant quoted by Brown and Prue, determined by two different methods at low ionic strengths, lies in the range 200—300. The measurements for cobalt thiosulphate show a very similar change with ionic strength.

[16] Denney and Monk, *Trans. Faraday Soc.*, 1951, **47**, 992.
[17] Davies, *J.*, 1938, 2093.
[18] Guggenheim, *Phil. Mag.*, 1935, **19**, 588.
[19] Brown and Prue, *Proc. Roy. Soc.*, 1935, **A**, **232**, 320.

constant obtained is constant over a wide range of chloride was considered proof that no other complexes needed to be considered:

Chloride concn.	0·41	0·63	0·81	0·98	1·40	1·82
Equilibrium const.	0·41	0·38	0·34	0·38	0·36	0·30

The molar extinction coefficient used for $CoCl_4^{2-}$ was 605 at 690 mμ. The ratio of the extinction coefficients at 690 mμ and 625 mμ, the region of the spectrum in which $CoCl_3$ or $CoCl_3^-$ complexes might be expected to absorb, was constant at 1·55 over a range of approximately 1000-fold change in absorption at these wavelengths. We take it that the amounts of complexes other than $CoCl^+$ and $CoCl_4^{2-}$ are negligible.

Discussion

The formation of thiocyanate, thiosulphate, and chloride complexes is accompanied by a change in the absorption spectra in the visible as well as in the ultraviolet spectrum. The change in position of a *d–d* band of a bivalent cation on complex formation should be about half that of a tervalent cation according to Owen's observations.[20] This relationship is roughly obeyed in a comparison between the data on the cobaltous and cobaltic ions, Tables 1 and 3 confirming that association is as complexes in these cases.

From a study with use of a cryoscopic method depending on the determination of activities, Brown and Prue [19] found that the thermodynamic stability constant of cobaltous sulphate association is $2{\cdot}3 \times 10^2$. Of course this study did not allow of a distinction between ion-pairs and complexes. The value is very similar to the thermodynamic stability constant found [16] for cobaltous thiosulphate, $1{\cdot}2 \times 10^2$, and as the two salts are electrolytes of the same charge type the same dependence of the association upon ionic strength is to be expected. Although very considerable changes in the absorption spectra of cobaltous solutions ($\mu = 1{\cdot}0$) were observed in the presence of thiosulphate, no spectrophotometric changes were found in the cobaltous sulphate solutions at the same ionic strength. We conclude that the association in the sulphate is of the ion-pair rather than the complex type. Confirmation of this can be obtained by studies with other cations.

In cupric perchlorate solutions to which sulphate is added the *d–d* band at ~800 mμ shifts to longer wavelengths and higher extinctions as expected for complex and not ion-pair formation.[22] The strength of this association is, within experimental error, the same as that in cobaltous solutions [19] but the cobaltous and the cupric solutions have different spectroscopic properties. It is interesting that cobaltous sulphate crystallises with an octahedron of water molecules about it whereas cupric sulphate crystallises with a sulphate anion in one of the six positions. The changes in absorption spectrum of the cupric sulphate solutions are towards the spectrum of the crystalline pentahydrate.[21] Only when cobaltous sulphate is in a solution of very strong sulphate concentration does the absorption at 515 mμ shift to longer wavelengths [23,24] and toward that of anhydrous cobaltous sulphate. We presume that at these concentrations the sulphate anions are adjacent to the cation. Though much of this evidence is circumstantial it points to the first association of cobaltous and sulphate ions as being of the ion-pair type. An entirely comparable series of observations has been made in nitrate solutions and we believe that the low activities of cobaltous nitrate solutions referred to earlier are due to ion-pair formation also as there is no indication of any complex. Earlier [11] we expressed the opinion that small cations form ion-pairs with sulphate and nitrate and that large cations form complexes. This assumption explained the anomalous stability orders of association of Group IIA cations with these anions. The present discussion confirms the earlier impression, cobaltous being considered a small cation. In the same paper we stated that hydration numbers of anions, as given by Stokes and Robinson,[24] must be in error as the

[20] Owen, *Discuss. Faraday Soc.*, 1955, **19**, 127.
[21] Bjerrum, Ballhausen, and Jørgensen, *Acta Chem. Scand.*, 1954, **8**, 1275.
[22] Nasanen, *Acta Chem. Scand.*, 1949, **3**, 179.
[23] Ballhausen and Jørgensen, *Acta Chem. Scand.*, 1955, **9**, 397.
[24] Stokes and Robinson, *J. Amer. Chem. Soc.*, 1948, **70**, 1870.

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calculation of them did not take into account the formation of ion-pairs and complexes in concentrated solutions of strong electrolytes. The relative hydration of cobaltous iodide and chloride was a case in point. We have now shown that cobaltous forms halide complexes in the stability order $Cl^- > I^-$. Unless account is taken of this association Stokes and Robinson's calculation leads to an anomalously higher hydration for iodide than chloride.

Cobaltous Complexes.—During this study interesting information has accumulated about cobaltous complexes. The first point is the stability order of anion complexes $ClO_4^- \leqslant I^- < Br^- < Cl^- < CNS^- < (CN^-)$, which appears to be quite general for first-row transition-metal cations. It is the order of the crystal-field splitting produced by these anions as found from the spectra of the complexes.

A second point concerns the extinction coefficients of the complexes. The extinction coefficient at the absorption maxima (Table 2) has the following values in CoX^- (ultraviolet in parentheses follows visible): Cl^-, 12·7 (?); SCN^-, 44·4 (1140); $S_2O_3^{2-}$, 375 (620).

The very sharp rise in extinction in the visible band of the thiosulphate is observed in ferric thiosulphate complexes too.[25] It does not appear in the nickel complex. We believe that the *d*–*d* transition has become mixed with a partial charge-transfer to the holes in the d_ϵ states of the cation.[25]

In the study of the cobaltous halides we have shown that although we can detect $CoCl(H_2O)_5^+$ and $CoCl_4^{2-}$ no intermediate complexes could be found spectrophotometrically. This suggests that the change from an octahedral to a tetrahedral complex occurs on the addition of the fourth chloride ion and that the complexes $CoCl_2(H_2O)_4$ and $CoCl_3(H_2O)_3^-$ are unstable as octahedra because of the size of the ligands and unstable as tetrahedra because of the weak polarisability of the water molecules.

INORGANIC CHEMISTRY LABORATORY, OXFORD. [*Received, July 23rd*, 1957.]

[25] Williams, *J.*, 1956, 8.

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82. *Further Complexes of Ferrous Dimethylglyoxime.*

By (the late) B. A. JILLOT and R. J. P. WILLIAMS.

Further complexes of ferrous dimethylglyoxime, $Fe(DMG)_2$, have been studied. The stability and absorption spectra of these complexes are compared with the corresponding properties of complexes of ferrous porphyrins. Like the latter, $Fe(DMG)_2$ has a greater affinity for cyanide and carbon monoxide than for ligands such as ammonia and pyridine. The affinity for both aliphatic and aromatic bases is independent of the basic strength of the ligands.

IN a search for models with similar physical properties, *e.g.*, absorption spectra and magnetic moments, to those of the iron porphyrin complexes we decided to study the properties of the further complexes of ferrous dimethylglyoxime. A series of such complexes will be briefly discussed here, leaving until later a detailed examination of the individual systems. The ferrous dimethylglyoxime complex itself, $Fe(DMG)_2$, is unstable even in the complete absence of oxygen unless a reducing agent and a base are also present. (The functions of both base and reducing agent can be fulfilled by hydrazine.) In the presence of this combination further complexes of the ferrous dimethylglyoxime with the bases are formed; their formulæ have been established [1,2,3] as $Fe(DMG)_2(Base)_2$. This stoicheiometry has been confirmed in the present work. The relative affinities of different bases for the ferrous dimethylglyoxine unit have been determined also.

The $Fe(DMG)_2$ *Complex with Hydrazine.*—Dimethylglyoxime is not very soluble in water. In order to work with its iron complex in the presence of excess of the reagent

[1] Griffing and Mellon, *Analyt. Chem.*, 1947, **19**, 1017.
[2] Banks and Byrd, *Analyt. Chim. Acta*, 1954, **10**, 129.
[3] Babko and Dubovenko, *J. Gen. Chem., U.S.S.R.*, 1954, **25**, 759.

25% aqueous dioxan was used as solvent. The ionic strength of all solutions in this solvent was kept at 0·3M by addition of appropriate amounts of sodium perchlorate. All measurements were made at 25°. Under these conditions the "practical" acid dissociation constant [4] of dimethylglyoxime is $pK = 12{\cdot}6 \pm 0{\cdot}1$, and that of hydrazine is $8{\cdot}15 \pm 0{\cdot}05$ as determined by pH titration against standardised sodium hydroxide. A comparison of the titration curve of 0·1M-hydrazine sulphate plus 5×10^{-3}M-dimethylglyoxime with the same titration in the presence of 10^{-3}M-ferrous ion showed that four protons are released by the ferrous ion on forming a complex. The reaction can be represented as

$$2N_2H_5^+ + 2DMGH_2 + Fe^{2+} \longrightarrow Fe(DMGH)_2(N_2H_4)_2 + 4H^+$$

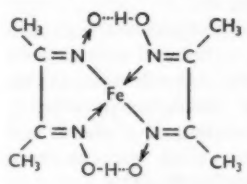
This agrees with the earlier work on the formula of the complex.[1,2,3] In the presence of a reducing agent which is not a base, *e.g.*, sodium formaldehydesulphoxylate, only a transient red colour was seen when the pH was raised rapidly to 7·0 before the brown ferric complex was formed. The transient species is very probably the unstable ferrous dimethylglyoxime complex $Fe(DMG)_2$, which begins to be formed at pH 7·0 and therefore has an overall stability constant, log K_2, of ~15. This value is of the expected order of magnitude relative to those of other transition-metal cations determined by us and by Freiser,[5] namely for Ni^{II}, 21·0; Cu^{II}, 22·5; Zn^{II}, 14·5; and Fe^{II}, 15·0.

The ferrous dimethylglyoxime complex with hydrazine has an intense absorption band, $\varepsilon_{max.} \sim 10^4$, in the visible region, $\lambda_{max.} = 525$ mμ (Table 1). This band is found in certain other ferrous complexes and does not belong to the ligand—it is absent in the other transition-metal cation complexes with dimethylglyoxime. The band has an intensity of $\varepsilon_{max.} = 10^4$ only in completely covalent diamagnetic ferrous complexes.[6] It will be assumed in what follows that the further complexes of ferrous dimethylglyoxime with bases (which have such strong absorption bands) are diamagnetic.

It is reasonable to suppose that the ferrous complex consists of a planar group of the cation and two dimethylglyoxime molecules, as is found in the nickel and cupric complexes.[7] This configuration is stabilised by hydrogen bonds (see inset). The second-step stability constant exceeds that of the first step in the formation of the cupric complex: this must be due to the hydrogen bonding.

If this structure is correct the two molecules of base must be added above and below the plane of the complex, as in the structure previously given.[8] Thus the complexes may well be very similar indeed to iron porphyrin proteins.

Evidence supporting the suggested structure has arisen through the study of the ferric dimethylglyoxime complexes. When alkali was added to ferric ions and dimethylglyoxime in acid solution a yellow complex was completely formed by pH 3·5 with the displacement of three protons. This complex was not formed when ferric dimethylglyoxime was prepared by the addition of alkali to ferrous ion and dimethylglyoxime in the presence of a reducing agent such as sodium formaldehydesulphoxylate at pH 6—7. The latter complex was fully formed, as measured by its absorption spectrum, when the ratio of ligand to iron was equal to or greater than 2 : 1 but the former complex was not. Moreover, the brown complex could not be obtained by starting from the ferric state. Both ferric complexes were formed with the displacement of three protons. The first is considered to be $Fe(DMG)_3$ and the second $Fe(DMG)_2(OH)(H_2O)$. It is difficult to reach any conclusion but that the second complex is formed directly from planar $Fe^{II}(DMG)_2$ which was seen as a transient red species at pH 6—7 in the preparation of the brown ferric compound.



[4] Irving and Rossotti, *J.*, 1954, 2910.
[5] Freiser, *Analyst*, 1952, **77**, 830.
[6] Williams, *J.*, 1955, 137.
[7] Godycki and Rundle, *Acta Cryst.*, 1953, **6**, 487.
[8] Welcher, "Organic Analytical Reagents," Vol. III, Van Nostrand Co. Inc., New York, 1947, p. 210.

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Exchange of Bases.—The hydrazine molecules which are bound to the $Fe(DMG)_2$ complex can be replaced by other bases. By carrying out competition exeriments between hydrazine and these bases in the solvent system described, and using the changes in absorption spectrum to follow the reactions, equilibrium constants K (Table 1) were obtained, where

$$K = [Fe(DMG)_2(N_2H_4)(base)][N_2H_4]/\{[Fe(DMG)_2(N_2H_4)_2][base]\}$$

Typical experimental data are given in Table 2. The constants refer to the replacement of only one hydrazine molecule of the two present in $Fe(DMG)_2(N_2H_4)_2$. This was established by the constancy of K at different hydrazine and base concentrations (see experimental data). The replacement of the second hydrazine molecule will be described later.

The affinity of a base for $Fe^{II}(DMG)_2$ is not related to its pK value. Usually, some relationship between relative stability (equilibrium) constants and pK values is found.

TABLE 1. *The equilibrium constants,* K, *and absorption spectra of the ferrous dimethylglyoxime complexes.*

Ligand	K	$\lambda_{max.}$ (mμ)	$\varepsilon_{max.}$	Ligand	K	$\lambda_{max.}$ (mμ)	$\varepsilon_{max.}$
$(N_2H_4)_2$	—	525	9,200	(N_2H_4)–CO ...	~1000	390	>5,000
(N_2H_4)Py	1·40 ± 0·10	510	8,900	(N_2H_4)–NH_2	—	527·5	9,100
		385	5,600	(N_2H_4)–Pr·NH_2	1·0 ± 0·5	535	9,050
$(N_2H_4)_2$–BrPy	1·24 ± 0·05	510	9,000	$(Py)_2$	—	512	9,200
	—	385	5,700			385	6,300
$(N_2H_4)_2$–CNPy	1·36 ± 0·14	505	13,500	(4-CNPy)$_2$ ...	—	495	9,500
		475 *	—			475 *	—
$(N_2H_4)_2$–CNPy	1·28 ± 0·05	508	7,200	$(Histidine)_2$ ...	—	525	4,500
		460	7,000	$(CN)_2$	—	375	6,000
(N_2H_4)–CN ...	820 ± 200	495	9,000	(Py)(CN)	—	490 †	9,000

Py = Pyridine, Pr = Propyl, CNPy = cyanopyridine, BrPy = bromopyridine.
* = Inflexion. † No second band.

In fact, here, pyridines have a slightly greater affinity than aliphatic bases despite pyridines' being weaker bases. Amongst pyridines there is surprisingly little selectivity. On the other hand, cyanide and carbon monoxide have a much higher affinity for the iron complex than any other ligand. Ferrous porphyrins also form very stable complexes with cyanide and carbon monoxide, whieh accounts for the very toxic properties of these molecules. In the treatment of the latter complexes it has been suggested that their stability arises from the donation of the d_ϵ electrons of the iron atom into the empty π states of the ligand. This type of double bond also stabilises ferrous dipyridyl and *o*-phenanthroline complexes or indeed any other complex between iron(II) and a conjugated base such as dimethylglyoxime. This interpretation being accepted, the equal stability of the pyridine and aliphatic base complexes can be explained as follows.

In the 3*d* states of diamagnetic ferrous ion there are six paired electrons which go into the three d_ϵ states. The remaining two d_γ states are empty and can be used as σ-electron acceptors. The strength of a bond from a base to the ferrous ion depends upon (1) its σ-donor strength, ammonia > pyridine, and (2) its π-acceptor strength, pyridine > ammonia. The two orders are opposed and explain the equal binding of aliphatic and aromatic bases. This series of stabilities illustrates, too, the increasing importance of d_ϵ-donor bonding as the charge on a cation is reduced, for ammonia binds singly and, to a greater degree, doubly charged cations much more strongly than pyridine. Amongst pyridines there is little difference in affinity for the ferrous complex. On the other hand, there are very great differences in absorption spectra between the different pyridine complexes which will now be described.

The Absorption Spectra of the $Fe(DMG)_2$ *Complexes.*—Table 1 lists the position of the absorption maxima in the different complexes of ferrous dimethylglyoxime. Amongst aliphatic bases the maximum moves to longer wavelengths as the strength of the base

increases. This order is the same as that observed by Griffing and Mellon [1] and by Sone [9] in similar series of complexes. These authors also observed that pyridine moves the absorption band to shorter wavelengths (Table 1). In the several pyridines used in the present study, the greater the π-electron-withdrawing character of the substituent the greater the shift of $\lambda_{max.}$ to shorter wavelengths. As further examples of this effect of π-electron-withdrawing groups the pyridine complexes can be compared with carbon monoxide and cyanide complexes. The latter move the absorption band to very short wavelengths. The following interpretation of the spectra is offered. In the absence of π-acceptor groups other than dimethylglyoxime, the d_ϵ electrons of ferrous ion form strong π-donor bonds from the cation to the dimethylglyoxime. The transition to the excited state involves the transfer of one of the d_ϵ electrons to a higher electron state of the ferrous ion, possibly $4p$, which interacts more strongly with the ligand. The electron is partially transferred to the ligand. This kind of electron transition is common to a large number of ferrous complexes.[6] When the $Fe(DMG)_2$ group is combined with unsaturated bases they stabilise the ground rather than the excited state, for such compounds also act as acceptors of the d_ϵ electrons which are responsible for the absorption. Thereby they reduce the ease of electron transfer to the dimethylglyoxime and the band moves to shorter wavelengths. On the other hand, π-electron-donor bases such as substituted amines shift the band to long wavelengths as they lower the relative stability of the ground state, repelling the d_ϵ electrons and facilitating charge transfer.

In the pyridine complexes, apart from the band at ~500 mμ, there is a band between 360 and 500 mμ, whose exact position depends upon the substituent in the pyridine. This band is at longer wavelengths for 4-cyanopyridine than in pyridine, 3-bromopyridine, or 3-cyanopyridine complexes. The explanation we offer for its appearance is that it is a charge-transfer band of a d_ϵ electron to the empty π-states of the pyridines. It moves to longer wavelengths in the 4-cyano-compound than in the other ligand complexes because of the greater electron-acceptor properties of this ligand.

Returning to the stability of the different pyridine complexes of ferrous dimethylglyoxime, we can interpret their almost equal stabilities consistently with our earlier remarks. The stability of the complex depends on the donor and acceptor character of the pyridines. The 4-cyanopyridine is the strongest π-electron acceptor but the weakest σ donor. Pyridine is a stronger σ-electron donor but a weaker π acceptor than the cyano-compounds. Similar stability of the different pyridine complexes arises through a balancing of the two parts of the bonding. It is surprising, however, that the two parts should so exactly compensate one another. The bonding through the d_ϵ-donor character of the ferrous ion has an important consequence in biological systems. If two kinds of ligand compete for the fifth and sixth positions of the co-ordination sphere of a cation in a complex, such as that of ferrous dimethylglyoxime, at a fixed pH then, because of the equal ability of the ligands to co-ordinate the ferrous ion, the weaker base, *i.e.*, the unsaturated compound, will be preferred. Thus in a biological system it is not surprising that ferrous porphyrins are further co-ordinated to glyoxalines and not to aliphatic amino-groups, for the glyoxalines have dissociation constants close to 7·0 whereas the amino-group constant is close to 9·0. The pH in a biological system is approximately 7·3.

Finally, we comment upon the rate at which the different complexes are formed. The reaction

$$Fe(DMG)_2(N_2H_4)_2 + \text{pyridine (py)} \longrightarrow Fe(DMG)_2(N_2H_4)(py) + N_2H_4 \quad . \; . \; . \quad (1)$$

is not instantaneous, implying once again that the ferrous complexes are inner orbital, *i.e.*, covalent and diamagnetic. The time for 50% conversion of one form into another is some 5 min. Now $Fe(DMG)_2(pyridine)_2$ has also been prepared and its properties examined. All its replacement reactions are exceedingly slow, so that oxidation occurs before exchange. The rate of reaction has been reduced by the d_ϵ–π double bonding. This is shown, too, in reaction (2) which is also very slow. If other bases are studied in place of

[9] Sone, *Bull. Chem. Soc. Japan*, 1952, **25**, 1.

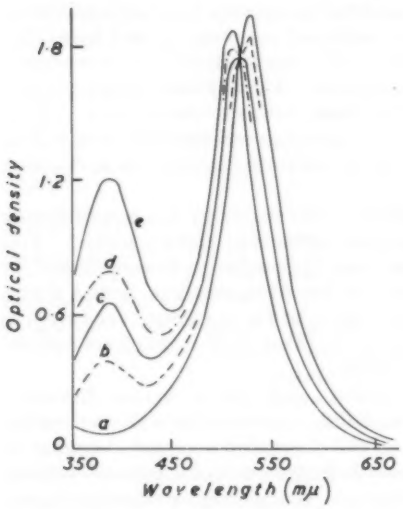
pyridine in reaction (1), the exchange of bases occurs at about the same rate, but if the base is unsaturated then the complex formed, *e.g.*, $Fe(DMG)_2(N_2H_4)CO$, reacts only slowly

$$Fe(DMG)_2(N_2H_4)(py) + py \longrightarrow Fe(DMG)_2(py)_2 + N_2H_4 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

with further base, *e.g.*, CO, and the reaction is only slowly reversible. These systems are being studied further as the parallel reactions of iron porphyrins are of great importance in biological systems.

Experimental

Materials.—Dioxan was purified by Weissberger and Proskauer's method.[10] " AnalaR " hydrated ferrous sulphate, potassium cyanide, and hydrazine hydrogen sulphate were used without further purification. Dimethylglyoxime was twice recrystallised from aqueous alcohol



Absorption spectra of ferrous dimethylglyoxime in the presence of 0·1M-*hydrazine sulphate at* pH 8·09 *together with different molarities of* 3-*bromopyridine*: (*a*) 0·00M, (*b*) 0·015M, (*c*) 0·036M, (*d*) 0·067M, (*e*) 0·95M; (*e*) *is taken to be the spectrum of the pure pyridine form.*

and then had the accepted m. p. 234°. It is often contaminated with small quantities of hydroxylamine. " AnalaR " pyridine was redistilled before use. Pure samples of substituted pyridines were given by Dr. A. R. Katritsky, whom we thank. Cylinder carbon monoxide was used without further purification.

Titrations.—All titrations were made at 25° in a thermostat, a Cambridge pH meter [4] being used. The calculation of the number of protons displaced in a given reaction was made from the difference in amounts of alkali required to reach a given pH in the presence and the absence of the cation. Suitable simple corrections were made for the dissociation of the ligand groups. Stability constants were obtained by the Bjerrum–Calvin method.[4] Acid dissociation constants are " practical " constants.[4]

Spectra.—All measurements were made in matched cells on a Unicam spectrophotometer S.P. 600. A typical set of observations is given in the Figure. Table 2 illustrates the accuracy of the calculation of equilibrium constants.

Table 2. *Equilibrium constant for the formation of the* 3-*bromopyridine complex.*

Concn. of 3-bromopyridine (mole/l.)	0·015	0·026	0·036	0·046	0·067
Optical density at 385 mμ	0·396	0·516	0·615	0·658	0·751
% of complex in pyridine form	29·9	40·9	50·1	53·9	62·4
Equilibrium constant	1·30	1·24	1·31	1·19	1·17

In this series of experiments the pH was buffered by the hydrazine (0·100M) at pH 8·09. The free hydrazine calculated from the dissociation constant given earlier was therefore

[10] Weissberger and Proskauer, " Organic Solvents," Oxford Univ. Press, 1935, p. 139.

0·0453M. All measurements were made in the solvent and salt background given on p. 463 and at 25°. Total ferrous ion (added as sulphate) was 10^{-3}M. Calculation of an equilibrium constant on the basis of the replacement of two hydrazine molecules by pyridine gives values ranging from 10·0 to 0·5. Similar results, not quoted, were obtained in all the other experiments. Saturated solutions of carbon monoxide were used to estimate the affinity of CO for the complex.

We thank The Royal Society for the gift of a Unicam Spectrophotometer S.P. 600.

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[*Received, August 7th*, 1957.]

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83. *Cyclic Keto-amines. Part III.* The Reactions of Substituted 1 : 2 : 3 : 4-Tetrahydro-4-oxoquinolines and of 1 : 6-Dioxojulolidines.*

By P. I. ITTYERAH and FREDERICK G. MANN.

Earlier studies of the reactions of the above two types of keto-amines have been extended. The structures of the derivatives formed by the action of *p*-nitrosodimethylaniline, by bromination, and by dehydrogenation have been elucidated. The action of hydrazine and of nitric acid, and the application of the Mannich and the Schmidt reaction, have also been investigated. The properties of 1 : 6-dioxo*iso*julоline are of particular interest.

THE preparation of 1 : 2 : 3 : 4-tetrahydro-4-oxo-1-phenylquinoline [1,2] (I; R = Ph) and its 1-methyl analogue [3] (I; R = Me), and that of the allied 1 : 6-dioxojulolidine [4] (II; R = R′ = H), with certain of their properties,[5–8] have been described. The most noteworthy properties of these cyclic keto-amines at present recorded concern the reactivity of the carbonyl groups. In the oxoquinoline derivatives (I; R = Ph or Me), this group reacts readily with appropriate amino-groups: it therefore forms a phenylhydrazone, and, in conjunction with the adjacent 3-methylene group, it undergoes the Pfitzinger reaction with alkaline isatin.[2,9] On the other hand, although the carbonyl group will readily condense with malononitrile to give a scarlet derivative,[10] no similar condensation has been achieved with other compounds having reactive methyl or methylene groups, such as quinaldine methiodide and 2-methylbenzothiazole ethiodide.

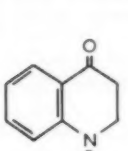
Similar properties are shown by the diketo-amine (II; R = R′ = H),[11] but, whereas this compound will condense with one or two equivalents of malononitrile, 7-methyl-1 : 6-dioxojulolidine (II; R = Me, R′ = H) will condense with only one equivalent, and the 7 : 9-dimethyl member (II; R = R′ = Me) does not condense.[10] The 7- and 9-methyl groups, in addition to showing this steric hindrance, can also activate the carbonyl groups. For example, the dioxojulolidines (II; R = R′ = H or Me) do not react with 2-methylbenzothiazole ethiodide under most rigorous conditions, but the 7-methyl member reacts with one equivalent of the ethiodide to give the cyanine iodide [12] (III).

In the present paper, a number of other reactions of these keto-amines are described.

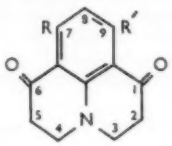
* Part II, Braunholtz and Mann, *J.*, 1957, 4166.

[1] R. C. Cookson and Mann, *J.*, 1949, 67.
[2] Mann, *ibid.*, p. 2816.
[3] Allison, Braunholtz, and Mann, *J.*, 1954, 403.
[4] Mann and Smith, *J.*, 1951, 1898.
[5] Braunholtz and Mann, *J.*, 1952, 3046.
[6] *Idem*, *J.*, 1953, 1817.
[7] *Idem*, *J.*, 1954, 651.
[8] *Idem*, *J.*, 1957, 4166.
[9] *Idem*, *J.*, 1955, 381.
[10] Ittyerah and Mann, *J.*, 1956, 3179.
[11] Braunholtz and Mann, *J.*, 1955, 393.
[12] *Idem*, *ibid.*, p. 398.

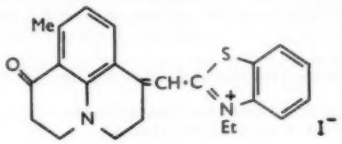
1 : 2 : 3 : 4-Tetrahydro-1-methyl-4-oxoquinoline (I; R = Me) with *p*-dimethylaminobenzaldehyde in boiling ethanol containing piperidine gives the bright red 3-(*p*-dimethylaminobenzylidene) derivative (IV). The oxoquinoline (I; R = Me) also condenses with



(I)

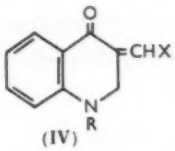


(II)

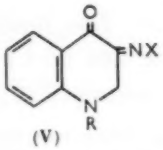


(III)

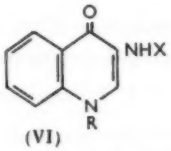
p-nitrosodimethylaniline in ethanol containing sodium hydroxide, apparently to give the analogous 3-(*p*-dimethylaminophenylimino)-derivative (V). This compound however forms deep yellow crystals, but in general compounds having the $\text{:N}\cdot C_6H_4\cdot NMe_2$ group are markedly deeper in colour than the analogous compounds having the $\text{:CH}\cdot C_6H_4\cdot NMe_2$



(IV)



(V)



(VI)

X = *p*-$NMe_2\cdot C_6H_4$

group. The infrared spectrum of the yellow crystals revealed two sharp strong bands at 3280 and 1627 cm.$^{-1}$, indicating an :NH group and a highly conjugated :CO group respectively, and there is little doubt that the imino-derivative (V) has isomerised to 3-(*p*-dimethylaminoanilino)-1 : 4-dihydro-1-methyl-4-oxoquinoline (VI; R = Me). The dark yellow 1-phenyl homologue has therefore the same structure (VI; R = Ph).

It is noteworthy that Leonard and Locke[13] have adduced evidence that various 1-methyl-4-oxo-3 : 5-dibenzylidenepiperidines (VIIA, where R is a *p*- or *m*-substituent),

(VIIA) (VIIB)

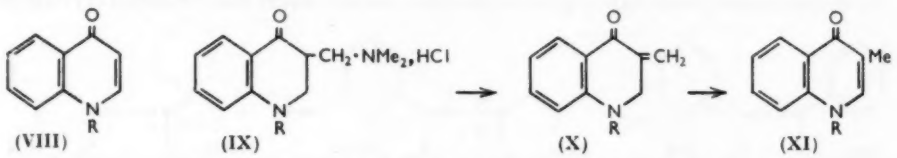
when heated with palladium–charcoal, preferably in ethylene glycol, undergo a similar conversion into the colourless 1 : 4-dihydro-pyridine isomers (VIIB). It is clear that under the far milder conditions of our condensations, the imino-compound (V) undergoes this isomerisation, whereas the highly coloured methylene compound (IV) does not.

Dehydrogenation of the oxoquinolines (I; R = Me and Ph) has been investigated both by attempted bromination in the 3-position with subsequent loss of hydrogen bromide, and by the action of palladised charcoal. The direct bromination of the oxoquinoline (I; R = Me) proved however to be unsatisfactory and a pure derivative was not isolated. *N*-Bromosuccinimide (1 or 2 equivalents) reacted with the oxoquinoline in cold carbon tetrachloride solution, to give the 6-bromo- and the 6 : 8-dibromo-derivative respectively, and no decisive evidence of bromination of the heterocyclic ring was obtained. The constitution of the lemon-yellow 6-bromo-derivative is confirmed by the following evidence: (*a*) it is unaffected by hot aqueous or ethanolic potassium hydroxide; (*b*) it forms a phenylhydrazone, and reacts with *p*-dimethylaminobenzaldehyde and with *p*-nitrosodimethylaniline to give a deep orange benzylidene derivative (as IV) and a yellow anilino-derivative (as VI) respectively; (*c*) its infrared spectrum shows a strong band at 813 cm.$^{-1}$ (12·30 μ) characteristic of 1 : 2 : 4-trisubstituted benzenes, and a band at 1672 cm.$^{-1}$ which

[13] Leonard and Locke, *J. Amer. Chem. Soc.*, 1955, **77**, 1852.

is normal for a :CO group directly conjugated to a benzene ring. The deep yellow 6 : 8-dibromo-derivative also has the chemical properties noted in (*a*) and (*b*).

The oxoquinoline (I; R = Ph) under the above conditions also gave the 6-bromo-derivative, having similar properties.



(VIII) (IX) (X) (XI)

The oxoquinolines (I; R = Me and Ph) were readily dehydrogenated by palladised charcoal in boiling ethylene glycol to 1 : 4-dihydro-1-methyl-4-oxoquinoline (echinopsine) (VIII; R = Me) and the 1-phenyl analogue (VIII; R = Ph) respectively. It is noteworthy that the 6-bromo-derivative of the oxoquinoline (I; R = Me) when similarly treated also gave the compound (VIII; R = Me).

The stability of the 1 : 4-dihydro-4-oxo-quinoline system is further emphasised by the application of the Mannich reaction to the oxoquinolines (I; R = Me and Ph). The

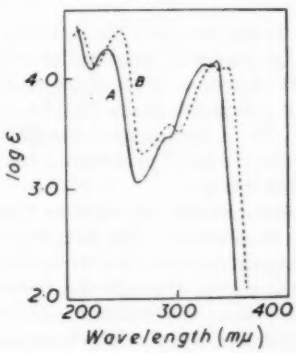


FIG. 1. *Absorption spectra in ethanol of* (*A*) 1 : 4-*dihydro*-1-*methyl*-4-*oxoquinoline* (VIII; R = Me) *and* (*B*) 1 : 4-*dihydro*-1 : 3-*dimethyl*-4-*oxoquinoline* (XI; R = Me).

oxoquinoline (I; R = Me), when dissolved in ethanol containing paraformaldehyde, dimethylamine hydrochloride, and a trace of hydrochloric acid, was recovered unchanged after the solution had been boiled for 4 hr. A similar mixture in *iso*pentyl alcohol gave a vigorous reaction on boiling, and deposited the pale yellow 1 : 4-dihydro-1 : 3-dimethyl-4-oxoquinoline (XI; R = Me). The evidence for this structure is summarised: (*a*) analysis and molecular-weight determination; (*b*) the compound shows no ketonic reactions, in common with the compound (VIII; R = Me); (*c*) the infrared spectrum shows a band at 1625 cm.$^{-1}$, indicating a highly conjugated :CO group joined to a benzene ring, but there is no band in the 890 cm.$^{-1}$ region and hence a :CH_2 group is absent; (*d*) the ultraviolet spectra of this compound and of (VIII; R = Me) are almost identical (Fig. 1).

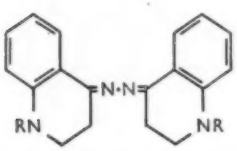
The oxoquinoline (I; R = Ph), similarly treated, gave the 1 : 4-dihydro-3-methyl-1-phenyl derivative (XI; R = Ph), which was also obtained when diethylamine hydrochloride was used in the reaction. There is little doubt therefore that the initial product in this reaction is the tertiary amine hydrochloride (IX), which breaks off the dialkylamine hydrochloride to form the 3-methylene derivative (X), which then isomerises to the stable 3-methyl derivative (XI).

The amines (I; R = Me and Ph) reacted readily with hydrazine in ethanolic solution to give the ketazines (XII; R = Me), orange plates, and (XII; R = Ph), golden-yellow crystals, respectively.

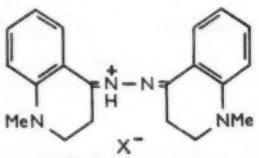
When the ketazine (XII; R = Me) was added to an excess of picric acid, both in cold

XUM

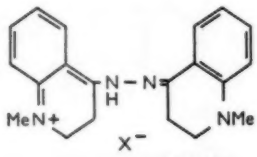
ethanolic solution, deep red crystals of the stable monopicrate were deposited. A chilled ethanolic suspension of the ketazine, when treated with hydrogen chloride, gave first a clear deep red solution which then deposited deep red crystals of a hydrochloride. The addition of cold concentrated hydrochloric acid to the red solution, before separation of the hydrochloride, immediately gave a colourless solution which then deposited crystalline



(XII)



(XIIIA)

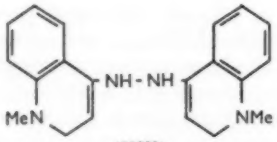


(XIIIB)

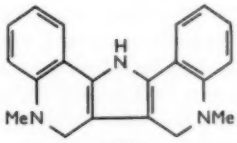
hydrazine dihydrochloride, demonstrating the ready hydrolysis of the ketazine in the presence of an excess of aqueous acid. The red crystalline hydrochloride of the ketazine was not obtained pure, for it could not be recrystallised, and was highly deliquescent, giving a red liquid which on exposure to air slowly evaporated, depositing the crude, dry yellow ketazine. Analysis indicated that the red crystals were probably a dihydrochloride.

If salt formation with the ketazine occurred by protonation of the MeN: group, no fundamental change in structure or colour would result. Consequently protonation must occur on the nitrogen of the azine chain, and the picrate will therefore be a cyanine salt, having the canonical forms (XIIIA—B). In the dihydrochloride this process may be duplicated, or, if the positive charge on the first nitrogen of the azine group tends to inactivate the second,[14] protonation may occur on this first nitrogen atom and on the more distant MeN: group.

Many unsuccessful attempts to convert the ketazine (XII; R = Me) into the indole (XV) have been made. The ketazine in boiling ethanolic hydrogen chloride or ethanolic acetic acid again underwent hydrolysis to the parent amine (I; R = Me). When hydrogen chloride was passed through the molten ketazine[15] at 190—200°, the almost colourless dihydrochloride of the isomeric *s*-bis-(1 : 2-dihydro-1-methyl-4-quinolyl)hydrazine (XIV) was obtained, and was further characterised by conversion into the yellow dipicrate.



(XIV)



(XV)

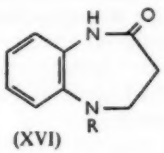
The oxoquinoline (I; R = Me) when subjected to the Schmidt reaction, by the addition of sulphuric acid and then sodium azide to its chilled chloroform solution, gave the colourless lactam (XVI; R = Me): the amine (I; R = Ph) behaved similarly. The precise structure of these lactams has not been determined, but by analogy with the results obtained by Briggs and De Ath[16] the structure (XVI) is more probable than the isomeric structure (XVII).

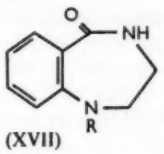
The oxoquinoline (I; R = Me), when treated with nitric acid–acetic acid below 15°, readily gave the 6-nitro-derivative (XVIII) in high yield.

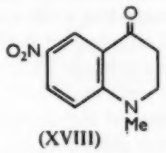
The chemistry of 1 : 6-dioxojulolidine (II; R = R′ = H) and its derivatives has been investigated on similar lines.

[14] Mann and Watson, *J. Org. Chem.*, 1948, **13**, 502.
[15] Robinson and Robinson, *J.*, 1918, **113**, 639.
[16] Briggs and De Ath, *J.*, 1937, 456.

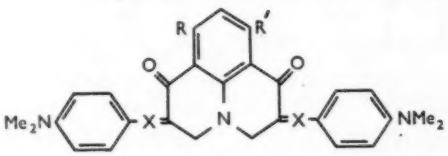
Braunholtz and Mann [12] have shown that this diketo-amine with *p*-dimethylaminobenzaldehyde and *p*-nitrosodimethylaniline gives the bright orange 2 : 5-bis-(*p*-dimethylaminobenzylidene) derivative (XIX; R = R′ = H, X = :CH·) and the bluish-purple

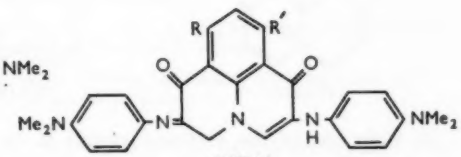

(XVI)


(XVII)


(XVIII)

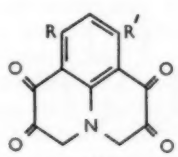
2 : 5-bis-(*p*-dimethylaminophenylimino)-derivative (XIX; R = R′ = H, X = :N·) respectively. We find that 7 : 9-dimethyl-1 : 6-dioxojulolidine (II; R = R′ = Me) condenses with these reagents to give the pale yellow derivative (XIX; R = R′ = Me, X = :CH·) and the dark purple derivative (apparently XIX; R = R′ = Me, X = :N·) respectively. These differences in colour between the two methin compounds (X = :CH·) on the one hand

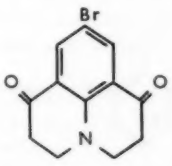

(XIX)

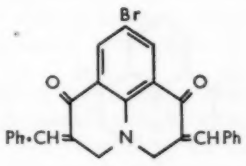

(XIXA)

and the two azomethin compounds (X = :N·) are to be expected on the basis of the above structures. We find however that the infrared spectra of the two azamethin compounds (XIX; R = R′ = H and Me, X = :N·) show marked absorption bands at 3280 and 3370 cm.$^{-1}$ respectively, and each compound must therefore have an :NH group. Hence there is little doubt that each compound has undergone isomerisation on one side only, to give the structure (XIXA), which is that of an *iso*juloline * derivative. The evidence for this limitation of the isomerisation is the intense, dark colours of the two compounds, for which, had the isomerisation occurred on both sides, there would have been no adequate structural basis: the reason for the limitation is the fact (discussed below) that the 1 : 6-dioxojulolidine structure can accept a double bond in the 2 : 3- or 4 : 5-position, but cannot accept this bond in both these positions, which of course is what the double isomerisation would entail.

The isomerisation is readily reversible, for the two azamethin compounds readily undergo acid hydrolysis to the brown 1 : 2 : 5 : 6-tetraoxojulolidine [12] (XX; R = R′ = H) and its 7 : 9-dimethyl homologue (XX; R = R′ = Me).


(XX)


(XXI)


(XXII)

The diketo-amine (II; R = R′ = H) also gave indefinite products on direct bromination. *N*-Bromosuccinimide in cold solution gave the yellow 8-bromo-1 : 6-dioxojulolidine (XXI). The position of the bromine atom is shown by the evidence: (*a*) the

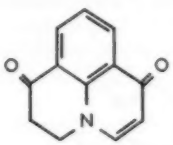
* For the nomenclature of unsaturated derivatives of julolidine, see refs. 4, 12.

compound is unaffected by hot aqueous-ethanolic potassium hydroxide; (*b*) it gives a yellow bisphenylhydrazone and with benzaldehyde a 2 : 5-dibenzylidene derivative (XXII); (*c*) its infrared spectrum is very similar to that of 8-chloro-1 : 6-dioxojulolidine, prepared by Braunholtz and Mann by cyclisation of *p*-chloro-*NN*-di-2-cyanoethylaniline.[7]

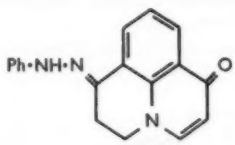
When however the yellow diketo-amine (II; R = R′ = H), m. p. 146°, was treated with palladised charcoal in boiling *p*-cymene, dehydrogenation occurred to give the colourless 1 : 6-dioxo*iso*juloline (XXIII), m. p. 202°, in 60% yield. Although the conditions of the experiment were varied over wide limits, no further dehydrogenation could be effected.

The properties of the *iso*juloline (XXIII) may be summarised.

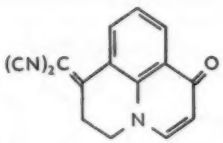
(i) Unlike the diketo-amine (II; R = R′ = H), which does not form stable salts with acids or apparently undergo quaternisation, the *iso*juloline (XXIII) forms a stable hydrobromide, picrate, and methotoluene-*p*-sulphonate. With perchloric acid, it forms a pale yellow salt of unusual composition, $(C_{12}H_9O_2N)_2,HClO_4$, which when treated with an excess of the acid gives the colourless normal salt, $C_{12}H_9O_2N,HClO_4$.



(XXIII)



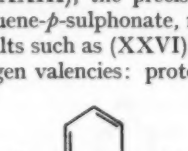
(XXIV)



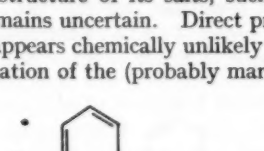
(XXV)

(ii) Only one of the carbonyl groups in the *iso*juloline has normal reactivity. For example, in the presence of an excess of reagent the *iso*juloline forms a scarlet monophenylhydrazone (XXIV), and a bright yellow condensation product (XXV) with one equivalent of malononitrile, whereas the diketo-amine (II; R = R′ = H) gives a yellow bisphenylhydrazone and a deep red product with two equivalents of malononitrile. The infrared spectra confirm this difference: the spectrum of the dioxojulolidine shows only one sharp band, at 1681 cm.$^{-1}$ (5·95 μ) associated with the :CO group, this value being normal for a carbonyl group joined to a benzene ring, but that of the dioxo*iso*juloline shows two such bands, at 1695 cm.$^{-1}$ (5·90 μ) and 1631 cm.$^{-1}$ (6·13 μ), the second being that of a carbonyl group joined to a benzene ring and having additional conjugation. Moreover the identity of the reactive carbonyl group is not in doubt, for the spectra of the monophenylhydrazone of the dioxo*iso*juloline and of the malononitrile derivative show only one carbonyl band at 6·16 and 6·12 μ respectively, which also confirms the structures (XXIV) and (XXV).

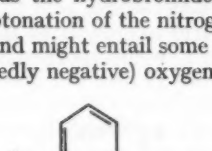
In spite of this clear spectral differentiation between the two :CO groups in the *iso*juloline (XXIII), the precise structure of its salts, such as the hydrobromide and the methotoluene-*p*-sulphonate, remains uncertain. Direct protonation of the nitrogen atom, to give salts such as (XXVI), appears chemically unlikely and might entail some strain on the nitrogen valencies: protonation of the (probably markedly negative) oxygen atom at



(XXVI)



(XXVIIA)



(XXVIIB)

the 1-position would give salts stabilised by the two forms (XXVIIA—B), of which form (B) has moreover acquired an extra aromaticised ring. Similar considerations apply to the quaternary salts. The infrared spectrum of the hydrobromide shows a broad band at 2690 cm.$^{-1}$, which might indicate a :NH$^+$ group or a heavily bonded OH group, and the

normal :CO band at 1710 cm.$^{-1}$, but the second :CO band is either absent or represented by a shoulder at 1625 cm.$^{-1}$, although this is almost overlaid by the conjugated aromatic band. The spectrum of the methotoluene-*p*-sulphonate gives no definite evidence for the :NMe$^+$ group, and shows the normal :CO band at 1708 cm.$^{-1}$, and again a faint shoulder at 1627 cm.$^{-1}$ largely obscured by the strong toluene-*p*-sulphonate absorption in this region.

FIG. 2. FIG. 3.

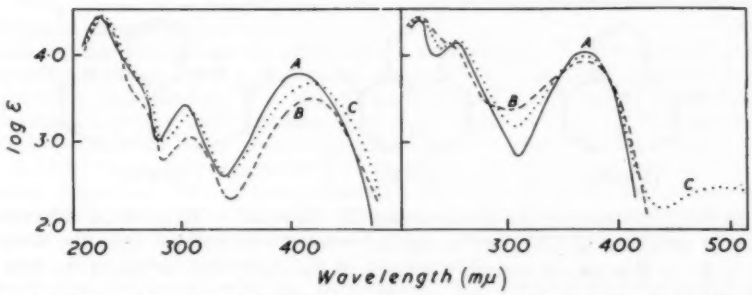


FIG. 2. *Absorption spectra of* 1 : 6-*dioxojulolidine* (II; R = R′ = H) *in* (*A*) *ethanol*, (*B*) 0·1N-*hydrochloric acid, and* (*C*) 0·1N-*aqueous potassium hydroxide.*

FIG. 3. *Absorption spectra of* 1 : 6-*dioxoisojuloline* (XXIII) *in* (*A*) *ethanol*, (*B*) 0·1N-*hydrochloric acid, and* (*C*) 0·1N-*aqueous potassium hydroxide.*

(iii) The *iso*juloline has, as expected, only one reactive methylene group, and hence with *p*-dimethylaminobenzaldehyde gives the 5-(*p*-dimethylaminobenzylidene) derivative.

(iv) The pale yellow colour of ethanolic solutions of the dioxojulolidine becomes rather darker on the addition of acids, but is unaffected by alkali, and the ultraviolet absorption spectra in the three types of solvent are very closely similar (Fig. 2). An ethanolic solution of the dioxo*iso*juloline is unaffected in colour by the addition of acids, but becomes intensely purple on the addition of concentrated aqueous potassium hydroxide.

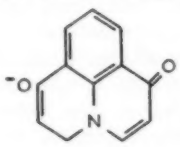
The ultraviolet spectra of the *iso*juloline (XXIII) in ethanolic and in acid and alkaline solution are shown in Fig. 3. The main absorption centred at 410 mμ shown by the dioxojulolidine is now shifted to 370 mμ for the *iso*juloline, but the spectrum of the latter in the alkaline solution shows a broad and novel band centred about 495 mμ which is responsible for the deep colour. The pure potassium derivative has not been isolated and its constitution remains uncertain: the purple derivative crystallises from cold concentrated aqueous-ethanolic potassium hydroxide, but is too deliquescent for collection. An ethanolic solution of the equimolecular mixture of the *iso*juloline and potassium hydroxide, when evaporated to dryness in a vacuum, gave a purple solid, the infrared spectrum of which indicated a mixture of the unchanged dioxo-compound and its potassium derivative: the use, in a similar experiment, of an excess of sodium methoxide in methanol to ensure complete conversion into the sodium derivative gave a solid hygroscopic purple deposit which was difficult to handle, and the infrared spectrum of which gave no decisive structural information.

It is unlikely that the anion (XXVIII) can produce this deep colour. Fission of the aryl–nitrogen bond in this anion to give the highly conjugated isomeric anion (XXIX) having marked resonance would almost certainly do so, but no evidence for this change could be obtained. The deep purple aqueous-ethanolic solution of the potassium derivative, when chilled and acidified, deposited the original dioxo*iso*juloline. Further, the anion (XXIX) on oxidation should give *iso*phthalic acid, but a solution of the *iso*juloline in aqueous sodium hydroxide, when oxidised with aqueous potassium permanganate, did not afford this acid.

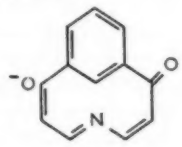
Addition of ethanolic ferric chloride to an ethanolic solution of the *iso*juloline

precipitated an unstable brown crystalline iron complex which redissolved in an excess of the chloride.

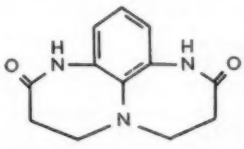
The dioxojulolidines (II; R = R′ = H and Me), unlike the oxo-amines (I), reacted with hydrazine to give amorphous stable, insoluble products which were probably complex. When suspensions of these products in ethylene glycol containing potassium hydroxide were heated, julolidine and its 7 : 9-dimethyl derivative respectively were formed in very low yield and isolated as their picrates.



(XXVIII)



(XXIX)

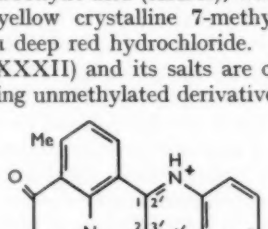


(XXX)

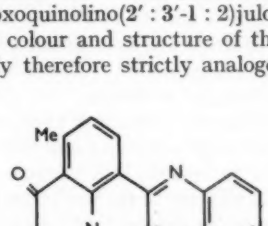
In the Schmidt reaction the dioxo-amine (II; R = R′ = H) gave the dilactam, most probably of structure (XXX), but no similar product was isolated from the dioxo-amine (II; R = R′ = Me), almost certainly because of the steric obstruction of the two methyl groups.

This steric obstruction arises also in the application of the Pfitzinger reaction to the 1 : 6-dioxojulolidines. Braunholtz and Mann [11] have shown that the parent compound (II; R = R′ = H) reacts with two equivalents of isatin in boiling alkaline solution, and the structures of the resulting zwitterionic dicarboxylic acid, and of the amine produced by its decarboxylation, have been extensively studied. 7-Methyl-1 : 6-dioxojulolidine, when similarly treated, afforded solely 7-methyl-6-oxoquinolino(2′ : 3′-1 : 2)juloline-4′-carboxylic acid, the deep purple colour of which showed that it had formed the zwitterion (XXXI). This condensation parallels that of 7-methoxy-1 : 6-dioxoarsulolidine, which with an excess of *o*-aminobenzaldehyde gave solely 7-methoxy-6-oxoquinolino(2′ : 3′-1 : 2)arsuloline.[17] 7 : 9-Dimethyl-1 : 6-dioxojulolidine, on the other hand, was unaffected by isatin in boiling alkaline solution, the two methyl groups completely obstructing the normal reaction.

The monocarboxylic acid (XXXI), when heated in a vacuum, underwent decarboxylation to the yellow crystalline 7-methyl-6-oxoquinolino(2′ : 3′-1 : 2)juloline (XXXII), which formed a deep red hydrochloride. The colour and structure of the acid (XXXI) and the base (XXXII) and its salts are clearly therefore strictly analogous to those of the corresponding unmethylated derivatives.[11]



(XXXI)



(XXXII)

1 : 6-Dioxojuloline (II; R = R′ = H) on nitration readily gave the 9-nitro-derivative. The reactions of this compound, and of the 6-nitro-oxoquinoline (XVIII) and its 1-phenyl analogue, are now being studied, particularly with regard to their reduction products.

Experimental

3-p-*Dimethylaminobenzylidene*-1 : 2 : 3 : 4-*tetrahydro*-1-*methyl*-4-*oxoquinoline* (IV; R = Me). —A solution of the oxoquinoline (I; R = Me) (0·3 g.) and *p*-dimethylaminobenzaldehyde (0·3 g., 2 mols.) in ethanol (15 c.c.) containing piperidine (0·1 c.c.), when boiled under reflux for 4 hr. and cooled, deposited the above *compound* as scarlet crystals (0·2 g., 36%), m. p. 145° after

[17] Mann and Wilkinson, *J.*, 1957, 3346.

crystallisation from ethanol (Found: C, 78·2; H, 6·8; N, 9·5. $C_{19}H_{20}ON_2$ requires C, 78·1; H, 6·85; N, 9·6%). The use of sodium hydroxide in place of piperidine gave only a sticky product in low yield.

A solution of the oxoquinoline (I; R = Ph) (0·3 g.) and the aldehyde (0·3 g.) in ethanol (5 c.c.) containing 10% aqueous sodium hydroxide (0·2 c.c.), when boiled for 1 hr. and set aside overnight, deposited the *1-phenyl analogue* (IV; R = Ph) (0·4 g.), pale yellow crystals, m. p. 148—150° (from acetone) (Found: C, 80·7; H, 6·3; N, 8·0. $C_{24}H_{22}ON_2$ requires C, 81·35; H, 6·2; N, 7·9%). The use of piperidine in place of sodium hydroxide in this experiment gave only unchanged oxoquinoline.

3-p-*Dimethylaminoanilino*-1 : 4-*dihydro*-1-*methyl*-4-*oxoquinoline* (VI; R = Me).—A solution of *p*-nitrosodimethylaniline (0·3 g., 2 mols.) in ethanol (5 c.c.) was added dropwise to a stirred solution of the oxoquinoline (I; R = Me) (0·3 g.) in ethanol (5 c.c.), diluted with 10% aqueous sodium hydroxide (2 c.c.), both solutions at 60°. The mixture when set aside deposited the *compound* (VI; R = Me), deep yellow needles, m. p. 215° (from ethanol) (Found: C, 73·6; H, 6·4; N, 14·2. $C_{18}H_{19}ON_3$ requires C, 73·7; H, 6·5; N, 14·3%): 0·5 g., 92%.

A similar experiment, with the oxoquinoline (I; R = Ph), deposited the *1-phenyl analogue*, a second crop being obtained by diluting the filtrate with water: the united crops, recrystallised from ethanol, afforded mustard-yellow crystals (0·6 g., 75%), m. p. 175° (Found: C, 77·6; H, 6·3; N, 11·5. $C_{23}H_{21}ON_3$ requires C, 77·7; H, 5·9; N, 11·8%).

A solution of the oxoquinoline (I; R = Ph) (0·7 g.), quinoline-2-aldehyde (0·5 g.), and potassium hydroxide (0·1 g.) in ethanol (15 c.c.), when boiled for 2 hr. and cooled, deposited the pale yellow *1-phenyl-3-2′-quinolylmethylene-4-oxo-derivative* (1 g.), m. p. 205° (Found: C, 83·1; H, 5·0; N, 7·6. $C_{25}H_{18}ON_2$ requires C, 82·9; H, 5·0; N, 7·7%).

Action of N-Bromosuccinimide.—(i) This reagent (1·7 g., 1 mol.) was added to a solution of the oxoquinoline (I; R = Me) (1·6 g.) in carbon tetrachloride (30 c.c.), which was vigorously shaken for 2 hr., filtered to remove deposited succinimide, and then evaporated under reduced pressure. The cold syrupy residue, which solidified when stirred, gave lemon-yellow 6-*bromo*-1 : 2 : 3 : 4-*tetrahydro*-1-*methyl*-4-*oxoquinoline*, m. p. 85° (from ethanol) (1·9 g., 78%) (Found: C, 50·3; H, 4·1; N, 5·7. $C_{10}H_{10}ONBr$ requires C, 50·0; H, 4·1; N, 5·8%). A solution of this compound in aqueous-ethanolic potassium hydroxide was boiled for 1 hr., and when poured into water deposited the unchanged compound.

This compound, treated with *p*-dimethylaminobenzaldehyde in ethanol containing piperidine as described above, gave the deep orange 3-p-*dimethylaminobenzylidene-derivative* (as IV), m. p. 165° (from benzene) (Found: C, 61·8; H, 4·8; N, 7·85. $C_{19}H_{19}ON_2Br$ requires C, 61·45; H, 5·1; N, 7·55%). A similar experiment, using *p*-nitrosodimethylaniline in ethanol containing 10% aqueous sodium hydroxide, afforded the yellow 3-p-*dimethylaminoanilino-derivative* (as VI), m. p. 281° (Found: C, 58·1; H, 4·5; N, 11·4. $C_{18}H_{18}ON_3Br$ requires C, 58·1; H, 4·8; N, 11·3%).

(ii) The oxoquinoline (I; R = Ph), similarly treated, gave the yellow 6-*bromo*-1 : 2 : 3 : 4-*tetrahydro*-1-*phenyl*-4-*oxoquinoline*, m. p. 95—100° (from ethanol) (Found: C, 59·3; H, 4·2; N, 4·8. $C_{15}H_{12}ONBr$ requires C, 59·6; H, 4·0; N, 4·6%), unaffected by boiling aqueous potassium hydroxide. It gave a pale orange 3-p-*dimethylaminoanilino-derivative* (as VI), m. p. 210° (from ethanol) (Found: C, 62·4; H, 4·8; N, 9·4. $C_{23}H_{20}ON_3Br$ requires C, 63·6; H, 4·6; N, 9·6%): low carbon values were obtained for this compound.

(iii) Experiment (i) was repeated, but *N*-bromosuccinimide (3·4 g., 2 mols.) and benzoyl peroxide (5 mg.) were used, the mixture being shaken for 4 hr. and set aside overnight. The residue from the filtered evaporated solution, when recrystallised from ethanol, gave the 6 : 8-*dibromo*-1-*methyl*-4-*oxo-derivative* (2·8 g., 88%), yellow needles, m. p. 126° (Found: C, 38·0; H, 3·0; N, 4·6. $C_{10}H_9ONBr_2$ requires C, 37·6; H, 2·8; N, 4·4%).

It gave a 3-p-*dimethylaminobenzylidene-derivative*, bright red plates, m. p. 190° (from benzene or methanol) (Found: C, 50·9; H, 3·75; N, 6·3. $C_{19}H_{18}ON_2Br_2$ requires C, 50·7; H, 4·0; N, 6·2%), and a bright yellow 3-p-*dimethylaminoanilino-derivative* (as VI), m. p. 225° (Found: C, 48·3; H, 3·9; N, 9·25. $C_{18}H_{17}ON_3Br_2$ requires C, 47·9; H, 3·8; N, 9·3%).

Dehydrogenation.—(i) A mixture of the oxoquinoline (I; R = Me) (1 g.), 10% palladised charcoal (0·1 g.) and ethylene glycol (10 c.c.) was boiled under reflux for 30 min. and filtered, the catalyst being then washed with the hot solvent. The combined filtrate and washings, when evaporated under reduced pressure, gave a brown viscous residue which readily crystallised. Its solution in ethanol, when treated with ethanolic picric acid, deposited the

yellow crystalline picrate[3] of 1 : 4-dihydro-1-methyl-4-oxoquinoline (VIII; R = Me), m. p. and mixed m. p. 226° (1·95 g., 80%).

(ii) Repetition of experiment (i), but using the 6-bromo-1-methyl-4-oxoquinoline, gave a brown viscous residue which readily solidified. It was soluble in water and contained ionic bromine. A portion, treated with picric acid, both in ethanol, afforded the above picrate, m. p. and mixed m. p. 226° (Found: C, 49·4; H, 3·0; N, 14·25. Calc. for $C_{10}H_9ON,C_6H_3O_7N_3$: C, 49·5; H, 3·1; N, 14·4%).

(iii) A similar experiment, using the oxoquinoline (I; R = Ph), afforded the pale greenish-yellow *picrate* of the 1-phenyl compound (VIII; R = Ph), m. p. 136° (from ethanol) (Found: C, 56·1; H, 2·85; N, 12·6. $C_{15}H_{11}ON,C_6H_3O_7N_3$ requires C, 56·0; H, 3·1; N, 12·45%).

The Mannich Reaction.—(i) A mixture of the oxoquinoline (I; R = Me) (0·8 g.), dimethylamine hydrochloride (0·6 g.), paraformaldehyde (0·2 g.), and *iso*pentyl alcohol (15 c.c.) was boiled under reflux for 15 min., and the clear yellow solution then treated with more aldehyde (0·3 g.), boiled for a further 30 min., and cooled. The yellow solid (0·8 g.) which separated was washed with hot ethanol, and when recrystallised from *iso*pentyl alcohol afforded the almost colourless crystalline 1 : 4-*dihydro*-1 : 3-*dimethyl*-4-*oxoquinoline* (XI; R = Me), m. p. 320° (decomp.) (Found: C, 76·6; H, 6·4; N, 8·2. $C_{11}H_{11}ON$ requires C, 76·3; H, 6·4; N, 8·1%). It was very sparingly soluble in boiling ethanol, acetone, and benzene. The ultraviolet spectrum is shown in Fig. 1.

(ii) Repetition of this experiment, but using the oxoquinoline (I; R = Ph) (1·1 g.), gave 1 : 4-*dihydro*-3-*methyl*-4-*oxo*-1-*phenylquinoline* (XI; R = Ph) which, on recrystallisation from *iso*pentyl alcohol, formed pale yellow crystals (1·0 g.) which when slowly heated darkened at 295° and slowly decomposed at 320—340°, but when immersed at 310° had m. p. 325° to a clear yellow liquid (Found: C, 82·0; H, 5·85; N, 6·2%; *M*, in boiling ethylene dibromide, 195. $C_{14}H_{13}ON$ requires C, 81·7; H, 5·5; N, 6·0%; *M*, 235).

Reactions with Hydrazine.—A solution of the oxoquinoline (I; R = Me) (0·8 g.) and pure hydrazine hydrate (0·12 g.) in ethanol (10 c.c.) containing acetic acid (0·1 c.c.) was boiled under reflux for 1 hr., crystals separating meanwhile. The deposit from the cold mixture, when collected and recrystallised from benzene, afforded NN′-*bis*-(1 : 2 : 3 : 4-*tetrahydro*-1-*methyl*-4-*quinolyl*)*diazine* (XII; R = Me) (0·75 g., 94%), bright orange plates, m. p. 198° (Found: C, 75·7; H, 6·8; N, 17·65. $C_{20}H_{22}N_4$ requires C, 75·5; H, 6·9; N, 17·6%).

Use of the oxoquinoline (I; R = Ph) in the above experiment afforded the golden-yellow 1-*phenyl analogue* (XII; R = Ph) (73%), m. p. 208° (from dioxan) (Found: N, 12·9. $C_{30}H_{26}N_4$ requires N, 12·7%).

Reactions of the Diazine (XII; R = Me).—(i) *Salt formation.* An ethanolic solution of the diazine, when added to a large excess of ethanolic picric acid, rapidly deposited the *monopicrate* (XIIIA–B; X = $C_6H_2O_7N_3$), very dark red needles, m. p. 165° (decomp.; immersed at 160°); the appearance and m. p. of the salt were unchanged by recrystallisation from hot ethanol (Found: C, 56·95; H, 5·0; N, 17·95. $C_{20}H_{22}N_4,C_6H_3O_7N_3$ requires C, 57·0; H, 4·6; N, 17·9%). An ethanolic suspension of the powdered diazine, when chilled to 0° and treated with a slow stream of dry hydrogen chloride, gave a clear deep red solution, from which red crystals separated. The mixture of solution and solute, when cautiously evaporated in an evacuated desiccator containing sodium hydroxide, gave fine deep red crystals of the hydrochloride. A portion of the red solution, before separation of the red crystals, was treated dropwise with cold concentrated hydrochloric acid; it became almost colourless and deposited hygroscopic crystals of hydrazine dihydrochloride, m. p. 198—200°, immersed at 180° (Found: H, 6·0; N, 27·5. Calc. for $H_4N_2,2HCl$: H, 5·8; N, 26·7%). Alternatively, a very fine suspension of the diazine in dry ether, when similarly treated with hydrogen chloride, was rapidly replaced by the deep red crystals, m. p. 85—87° (immersed at 60°) after decantation of the ether and rapid drying in a vacuum: analysis indicated these were apparently a dihydrochloride (Found: N, 14·3; Cl, 17·9. Calc. for $C_{20}H_{22}N_4,2HCl$: N, 14·3; Cl, 18·1%), but the composition varied with the age of the specimen. A sample when exposed to the air rapidly formed a red liquid which ultimately gave the crude dry ketazine, m. p. 180—189°.

(ii) *Attempted indolisation.* Hydrogen chloride was passed through the molten diazine initially at 200° and then at 190—200° for 30 min., the melt becoming red and viscous. An ethanolic solution of the cold product was filtered and diluted with considerable ether. The precipitated colourless crystals of the *dihydrochloride* of s-*bis*-(1 : 2-*dihydro*-1-*methyl*-4-*quinolyl*)-*hydrazine* (XIV), when collected, washed with ether–acetone, and dried had m. p. 295°

(decomp.), which varied with the rate of heating (Found: C, 60·7; H, 6·3; N, 13·9. $C_{20}H_{22}N_4,2HCl$ requires C, 61·4; H, 6·1; N, 14·3%).

This salt, treated in ethanol with picric acid, deposited the deep yellow *dipicrate*, m. p. 243° (decomp.) (from ethanol) (Found: C, 49·9; H, 3·4; N, 17·6. $C_{20}H_{22}N_4,2C_6H_3O_7N_3$ requires C, 49·6; H, 3·6; N, 18·0%).

Schmidt Reaction.—(i) Concentrated sulphuric acid (8 c.c.) was added dropwise to a stirred solution of the oxoquinoline (I; R = Me) (1·6 g.) in dry chloroform (10 c.c.) chilled in ice-water, and sodium azide (1·6 g., 2·5 mols.) was then added during 30 min. The solution was stirred for a further 15 min., diluted with ice-water (45 c.c.), neutralised with potassium carbonate, and extracted with ether. The extract, when dried (K_2CO_3) and evaporated, left a white residue, which on recrystallisation from benzene afforded the β-(N-o-*aminophenyl*-N-*methylamino*)-*propionic lactam* (XVI; R = Me) (1 g., 57%), needles, m. p. 170° (Found: C, 68·5; H, 6·7; N, 15·4. $C_{10}H_{12}ON_2$ requires C, 68·1; H, 6·8; N, 15·9%).

(ii) The oxoquinoline (I; R = Ph), similarly treated, afforded colourless β-(N-o-*aminophenylanilino*)*propionic lactam* (XVI; R = Ph), (91%), m. p. 221° after crystallisation from ethanol and then benzene (Found: C, 75·9; H, 6·1; N, 11·8. $C_{15}H_{14}ON_2$ requires C, 75·6; H, 5·9; N, 11·8%).

Nitration.—A mixture of concentrated nitric acid (1 c.c.) and acetic acid (10 c.c.) was added dropwise to a solution of the oxoquinoline (I; R = Me) (1 g.) in acetic acid (10 c.c.) at <15°. The mixture was set aside for 20 min. and then poured into water (50 c.c.). The crystalline precipitate afforded the 6-*nitro-derivative* (1·2 g., 93%), yellow needles, m. p. 169° (from ethanol) (Found: C, 58·5; H, 4·8; N, 13·6. $C_{10}H_{10}O_3N_2$ requires C, 58·25; H, 4·85; N, 13·6%). The compound gave a *phenylhydrazone*, bright red plates, m. p. 198° (decomp.) (from ethanol) (Found: C, 64·4; H, 5·2; N, 18·8. $C_{16}H_{16}O_2N_4$ requires C, 64·9; H, 5·4; N, 18·9%), and a 3-p-*dimethylaminobenzylidene derivative* (prepared in the presence of piperidine), red plates, m. p. 210° (from ethanol) (Found: C, 67·8; H, 5·4; N, 12·3. $C_{19}H_{19}O_3N_3$ requires C, 67·7; H, 5·6; N, 12·5%).

Cyanoethylation.—*p*-Chloroaniline on cyanoethylation gives a low yield of *p*-chloro-*NN*-bis-2-cyanoethylaniline,[5,6] which in turn on cyclisation gives a small yield of 8-chloro-1 : 6-dioxojulolidine.[7] This difficulty applies also to the bromo-analogues, but *p*-bromo-*NN*-bis-2-cyanoethylaniline and 8-bromo-1 : 6-dioxojulolidine can be readily prepared by direct bromination with *N*-bromosuccinimide.

p-*Bromo*-NN-*bis*-2-*cyanoethylaniline.*—(i) A mixture of *p*-bromoaniline (17 g.), vinyl cyanide (12 g., 2·25 mols), acetic acid (12 g.), and cuprous chloride (1·7 g.) was boiled gently under reflux for 12 hr. and then poured with stirring into ammonia (100 c.c.; *d* 0·88). The precipitated dark oil solidified when stirred and was collected and recrystallised from ethanol (charcoal), giving a crude almost colourless product, m. p. 75—90°. Fractional distillation gave p-*bromo*-N-2-*cyanoethylaniline*, b. p. 160°/5 mm., m. p. 96—98° (from ethanol) (Found: C, 47·9; H, 4·0; N, 12·3. $C_9H_9N_2Br$ requires C, 48·0; H, 4·0; N, 12·45%). The residue in the flask decomposed at higher temperatures.

This experiment, when repeated with boiling for 20 hr., gave on distillation a low-boiling fraction of the above compound (2 g.) and a crude higher fraction, b. p. 180—200°/0·5 mm., which after several laborious recrystallisations from ethanol gave p-*bromo*-NN-*bis*-2-*cyanoethylaniline* (4 g., 14%), m. p. 94—95° (Found: C, 51·8; H, 4·0; N, 15·1. $C_{12}H_{12}N_3Br$ requires C, 51·8; H, 4·3; N, 15·1%).

(ii) *NN*-Bis-2-cyanoethylaniline, when treated in carbon tetrachloride with *N*-bromosuccinimide (1 mol.) and benzoyl peroxide (0·05 mol.) for 4 hr. and worked up as previously described, gave the above *p*-bromo-derivative (82%), m. p. and mixed m. p. 95° (Found: N, 15·45%).

Attempted Cyclisation.—*p*-Bromo-*NN*-bis-2-cyanoethylaniline was heated with aluminium chloride in chlorobenzene, and the mixture worked up as described earlier.[5] The crude yellow solid, m. p. 79—81°, was apparently 1-2′-cyanoethyl-1 : 2 : 3 : 4-tetrahydro-4-oxoquinoline (I; R = ·C_2H_4·CN) (lit.,[18] m. p. 79—79·5°), for it gave a pale yellow *phenylhydrazone*, m. p. 250° (Found: C, 75·25; H, 6·0; N, 19·4. $C_{18}H_{18}N_4$ requires C, 74·7; H, 5·9; N, 19·4%), and a 2 : 4-*dinitrophenylhydrazone*, m. p. >360° (Found: N, 22·15. $C_{18}H_{16}O_4N_6$ requires N, 22·1%). Under the conditions employed for this monocyclisation the nuclear bromine had therefore been removed.

[18] Johnson and DeAcetis, *J. Amer. Chem. Soc.*, 1953, **75**, 2766.

Derivatives of 1 : 6-*Dioxojulolidine.—Quinoline-2-aldehyde derivatives.* A mixture of the diketone (II; R = R′ = H), the aldehyde (0·6 g.), ethanol (15 c.c.), and potassium hydroxide (0·1 g.) was boiled under reflux for 1 hr., and on cooling deposited crystals and some tar. Recrystallisation of the deposit from benzene afforded pale yellow 1 : 6-*dioxo*-2 : 5-*di*-(2-*quinolylmethylene*)*julolidine* (0·3 g.), m. p. 185° (Found: N, 8·7. $C_{32}H_{21}O_2N_3$ requires N, 8·8%).

The 7 : 9-dimethyl diketone (II; R = R′ = Me), similarly treated, gave the pale yellow 7 : 9-*dimethyl homologue*, m. p. 225° (from benzene) (Found: C, 80·3; H, 5·1; N, 8·4. $C_{34}H_{25}O_2N_3$ requires C, 80·4; H, 4·9; N, 8·3%).

The 7 : 9-dimethyl diketone, when treated with *p*-dimethylaminobenzaldehyde (2·2 mols.) in boiling alkaline ethanol, as previously described, gave 2 : 5-*bis*-p-*dimethylaminobenzylidene*-7 : 9-*dimethyl*-1 : 6-*dioxojulolidine* (XIX; R = R′ = Me, X = :CH·), (93%), pale yellow needles, m. p. 245° (from ethanol) (Found: C, 78·5; H, 6·6; N, 8·7. $C_{32}H_{33}O_2N_3$ requires C, 78·2; H, 6·7; N, 8·55%).

The 7 : 9-dimethyl diketone, similarly treated with *p*-nitrosodimethylaniline (2·1 mols.), afforded 2-p-*dimethylaminoanilino*-5-(p-*dimethylaminophenylimino*)-7 : 9-*dimethyl*-1 : 6-*dioxojulolidine* (XIXA; R = R′ = Me) (83%), which formed dark purple crystals, m. p. 268° (decomp.), from much acetone (Found: C, 73·2; H, 6·3; N, 14·2. $C_{30}H_{31}O_2N_5$ requires C, 73·0; H, 6·3; N, 14·2%). A solution of this compound (0·5 g.) in concentrated hydrochloric acid (20 c.c.) was boiled under reflux for 30 min., the deep red solution becoming brown and depositing 7 : 9-*dimethyl*-1 : 2 : 5 : 6-*tetraoxojulolidine* (XX; R = R′ = Me) (1·25 g.) as bronze-coloured crystals, which when collected and washed with water and then with boiling ethanol, benzene, and acetone, slowly decomposed above 330° (Found: C, 66·5; 64·6; H, 4·3, 4·3; N, 5·5. $C_{14}H_{11}O_4N$ requires C, 65·4; H, 4·3; N, 5·45%. The carbon value varied with the temperature and time of the combustion). This compound resembles the parent member (XX; R = R′ = H) in that it is insoluble in all the usual boiling solvents, but dissolves in aqueous potassium hydroxide to give an intense purple solution from which it is reprecipitated on acidification, and it does not condense with *p*-phenylenediamine.

Bromination.—N-Bromosuccinimide (2 g., 2 mols.) and benzoyl peroxide (0·05 g.) were added to a solution of the diketone (II; R = R′ = H) (1 g.) in carbon tetrachloride, which was then shaken vigorously for 3 hr. The yellow precipitate, when twice recrystallised from ethanol to remove succinimide and bromosuccinimide, gave 8-*bromo*-1 : 6-*dioxojulolidine* (XXI) (1·2 g., 86%), golden-yellow plates, m. p. 208° (Found: C, 51·2; H, 3·3; N, 5·1. $C_{12}H_{10}O_2NBr$ requires C, 51·4; H, 3·6; N, 5·0%). The ultraviolet spectrum in ethanol gave the following values (ε values in parentheses): $\lambda_{max.}$ 421·5—425·5 (5130); 301—302·5 (4490); 227 (30,100); $\lambda_{min.}$ 338·5—340 (252); 276·5 (1650).

When the above reaction mixture was boiled under reflux, only a pale brown amorphous intractable material was obtained.

The compound (XXI) gave a yellow crystalline *bisphenylhydrazone*, m. p. 270° (Found: C, 62·5; H, 4·7; N, 15·3. $C_{24}H_{22}N_5Br$ requires C, 62·6; H, 4·8; N, 15·2%). A mixture of the compound (XXI) (0·28 g.) and benzaldehyde (0·22 g., 2 mols.) in ethanol (15 c.c.) and piperidine (0·1 c.c.), when boiled under reflux, deposited deep red crystals of 2 : 5-*dibenzylidene*-8-*bromo*-1 : 6-*dioxojulolidine* (XXII) (0·2 g.), m. p. 200° (from ethanol) (Found: C, 68·0; H, 4·2; N, 3·4. $C_{26}H_{18}O_2NBr$ requires C, 68·4; H, 3·9; N, 3·1%).

When the diketone (II; R = R′ = H) was treated with *N*-chlorosuccinimide (1 mol.) under the above conditions, no reaction occurred at room temperature, but when the mixture was boiled under reflux for 1 hr. a sticky solid was deposited and after repeated recrystallisation from ethanol afforded 8-chloro-1 : 6-dioxojulolidine (68%), m. p. and mixed m. p.[7] 201°.

Dehydrogenation.—A mixture of the diketone (II; R = R′ = H) (1 g.), 10% palladised charcoal (0·1 g.) and *p*-cymene (25 c.c.) was boiled under reflux for 90 min., a slow stream of carbon dioxide being blown through the solution. The hot mixture when filtered and cooled deposited 1 : 6-*dioxoisojuloline* (XXIII), which recrystallised from dry benzene as colourless needles (0·6 g.), m. p. 202° (Found: C, 72·6, 72·3; H, 4·5, 4·5; N, 7·1%; *M* in boiling ethanol, 188. $C_{12}H_9O_2N$ requires C, 72·4; H, 4·5; N, 7·0%; *M*, 199). Lower yields were obtained in experiments on a larger scale.

Hydrobromic acid (1 c.c.; 48%) was added to a stirred solution of the *iso*juloline (0·1 g.) in ethanol (2 c.c.), which was then diluted with ether. The white crystalline precipitated *hydrobromide*, when collected and washed with ethanol–ether, had m. p. 270° (decomp.) (Found: C, 51·8; H, 3·7; N, 5·2. $C_{12}H_9O_2N,HBr$ requires C, 51·4; H, 3·6; N, 5·0%).

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The *iso*juloline and picric acid, when mixed in ethanolic solution, deposited the *picrate* as yellow needles, m. p. 202° after recrystallisation from ethanol (Found: C, 50·95; H, 3·0; N, 12·95. $C_{12}H_9O_2N,C_6H_3O_7N_3$ requires C, 50·5; H, 2·8; N, 13·1%). A mixture of the *iso*juloline and its picrate melted at *ca.* 170—175°.

Perchloric acid (0·1 c.c.; 60%) when added to a solution of the *iso*juloline (0·1 g.) in ethanol (5 c.c.) gave a thick pale yellow curdy precipitate of the *bis*-(1 : 6-*dioxo*isojuloline) *perchlorate*, m. p. 240° (decomp.), unchanged by crystallisation from ethanol (diamond-shaped crystals) or from water (needles) (Found: C, 58·1; H, 3·7; N, 5·8; Cl, 7·0. $2C_{12}H_9O_2N,HClO_4$ requires C, 57·8; H, 3·8; N, 5·6; Cl, 7·1%). A cold aqueous suspension of this salt when treated with aqueous ammonia deposited the *iso*juloline. An ethanolic solution of the salt, when treated with an excess of perchloric acid and set aside at 0° overnight, deposited colourless hygroscopic needles of the normal *perchlorate*, m. p. 125° (Found: N, 4·3. $C_{12}H_9O_2N,HClO_4$ requires N, 4·7%): these crystals dissolved in hot ethanol to give yellow solution, which on cooling deposited pale yellow crystals, m. p. 240° (decomp.), of the first salt.

A mixture of the *iso*juloline (0·1 g.) and methyl toluene-*p*-sulphonate (0·1 g.) when heated at 150° for 30 min. formed a clear red liquid which solidified on cooling. An ethanolic solution of this product was diluted with ether, whereby the colourless crystalline *methotoluene-p-sulphonate* was precipitated, and when collected and washed with ether–acetone had m. p. 180° (decomp.) (Found: N, 3·5. $C_{20}H_{19}O_5NS$ requires N, 3·6%).

The *phenylhydrazone* (XXIV) crystallised from methanol as a *hemihydrate*, scarlet plates, m. p. 220° (Found: C, 72·4, 72·5; H, 5·45, 5·6; N, 14·2. $C_{18}H_{15}ON_3,\frac{1}{2}H_2O$ requires C, 72·5; H, 5·4; N, 14·1%). The crystals when crushed on a porous plate formed a reddish-brown powder. 2-p-*Dimethylaminobenzylidene*-1 : 6-*dioxo*isojulolidine, prepared in boiling ethanol with piperidine, formed deep red crystals, m. p. 230°, from dioxan (Found: C, 76·0; H, 5·4; N, 8·8. $C_{21}H_{18}O_2N_2$ requires C, 76·5; H, 5·45; N, 8·5%).

A mixture of the *iso*juloline (0·33 g.), malononitrile (0·22 g., 2 mols.), ammonium acetate (0·1 g.), dry benzene (10 c.c.), and acetic acid (1 c.c.) was boiled under reflux for 45 min. in a flask fitted with a constant water-separator,[19] bright yellow crystals separating after 15 min. The crystals from the cold mixture were collected and recrystallised from ethanol and then acetic acid, affording 1-*dicyanomethylene*-6-*oxo*isojuloline (XXV), deep yellow needles, m. p. 245° (decomp.) (Found: C, 73·3; H, 3·8; N, 16·5. $C_{15}H_9ON_3$ requires C, 72·9; H, 3·6; N, 17·0%).

Attempted application of the Mannich reaction to the diketone (II; R = R′ = H) under the conditions described above gave solely an intractable pale-brown amorphous powder of indefinite m. p.

Action of Hydrazine.—(i) An ethanolic solution of the diketone (II; R = R′ = H) (2 mols.), hydrazine hydrate (1 mol.), and a few drops of acetic acid, when heated, deposited a complex orange polymeric mixture, m. p. 280—320°, from which no pure constituent could be isolated. The diketone (II; R = R′ = Me) gave a deep yellow mixture having similar properties.

(ii) To investigate reduction under the Wolff–Kishner conditions, a mixture of the diketone (II; R = R′ = Me) (1 g.), 100% hydrazine hydrate (1 g.), potassium hydroxide (0·5 g.), and ethylene glycol was boiled under reflux for 2 hr. and then heated at 195—200° for 4 hr., during which much of the initial orange precipitate decomposed. The mixture was diluted with water, cooled, and filtered. The collected material was dried and extracted with ethanol. The extract when evaporated afforded a brown solid, which, when redissolved in ethanol and treated with picric acid, gave in small yield a yellowish-orange picrate, almost certainly julolidine picrate: after crystallisation from ethanol this salt had m. p. 165° on slow heating, and m. p. 172° when immersed at 160° (lit.,[19,20] 165°, 174°).

The diketone (II; R = R′ = Me), similarly treated, afforded also in small yield yellow-orange 7 : 9-*dimethyljulolidine picrate*, m. p. 160° after crystallisation from ethanol (Found: C, 55·6; H, 4·8; N, 13·0. $C_{14}H_{19}N,C_6H_3O_7N_3$ requires C, 55·7; H, 5·1; N, 13·0%).

Schmidt Reaction.—The diketone (II; R = R′ = H), when treated in chloroform with sulphuric acid and sodium azide, precisely as described above, gave the *dilactam* (XXX) of 2 : 6-diamino-*NN*-di-2′-carboxyethylaniline (81%), which formed colourless plates, m. p. 356° (decomp.), from acetic acid (Found: C, 62·6; H, 5·25; N, 17·6. $C_{12}H_{13}O_2N_3$ requires C, 62·3; H, 5·5; N, 18·2%).

[19] Pinkus, *Ber.*, 1892, **25**, 2802; von Braun, Heider, and Wyczatkowsa, *Ber.*, 1918, **51**, 1224.
[20] Smith and Yu, *J. Amer. Chem. Soc.*, 1952, **74**, 1096.

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Pfitzinger Reaction.—A solution of 7-methyl-1 : 6-dioxojulolidine (II; R = Me, R′ = H) (2·1 g.), isatin (3·1 g., 2·1 mols.), and potassium hydroxide (3·6 g.) in methanol (25 c.c.) and water (5 c.c.) was boiled under reflux for 20 hr., and then filtered into a stirred solution of acetic acid (40 c.c.) in water (160 c.c.). The deep purple precipitated *7-methyl-6-oxoquinolino-(2′ : 3′-1 : 2)juloline-4′-carboxylic acid* (XXXI) (3 g., 87%), when collected, washed with hot ethanol, and dried, had m. p. 215° (decomp.) (Found: C, 73·3; H, 4·6. $C_{21}H_{16}O_3N_2$ requires C, 73·2; H, 4·65%. High nitrogen values were obtained). Its low solubility in boiling solvents precluded recrystallisation.

The acid, when heated in a tube at 210—220°/0·1 mm., underwent decarboxylation and gave a bright orange sublimate, which on crystallisation from ethanol afforded *7-methyl-6-oxoquinolino(2′ : 3′-1 : 2)juloline* (XXXII), bright yellow plates, m. p. 185°, unchanged by further crystallisation or sublimation (Found: C, 79·8; H, 5·2; N, 9·4, 9·45. $C_{20}H_{14}ON_2$ requires C, 80·0; H, 5·3; N, 9·3%).

Nitration.—Concentrated nitric acid (1 c.c.) was added dropwise to a solution of the diketone (II; R = R′ = H) (1 g.) in acetic acid (10 c.c.) at <20°; yellow crystals separated. The mixture was set aside for 20 min. and then poured into water (50 c.c.). The precipitate, after crystallisation from ethanol, afforded *8-nitro-1 : 6-dioxojulolidine* (1·2 g., 100%), golden-yellow needles, m. p. 250° (Found: C, 58·5; H, 4·2; N, 11·2. $C_{12}H_{10}O_4N_2$ requires C, 58·55; H, 4·1; 11·4%). The *bisphenylhydrazone*, prepared in the usual manner, formed deep red crystals, m. p. 270° (decomp.), insoluble in the common organic solvents (Found: C, 67·2; H, 5·0; N, 19·5. $C_{24}H_{22}O_2N_6$ requires C, 67·6; H, 5·2; N, 19·7%).

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84. *The Quenching of the Fluorescence of Anthracene*

By W. H. MELHUISH and W. S. METCALF.

The quenching of the fluorescence of anthracene by alkyl and aryl bromides and by some other halides is enhanced by electron-attracting substituents in the quenchers.

BOWEN and his collaborators[1,2,3,4,5] measured the quenching of the fluorescence of anthracene by many substances, in various solvents and over a wide range of temperatures, and examined the applicability thereto of various expressions based on diffusion theory.[2] Whereas quenching by many of the stronger quenchers is limited[1] by the rate of diffusion together of the excited anthracene and the quencher molecules,[4] quenching by the weaker quenchers is not so limited except in very viscous solvents such as medicinal paraffin or glycerol.[6]

In dilute solutions such weak quenching is sufficiently described[6] by the equation

$$(f_0/f - 1)/[Q] = k = \tau_0 k_3 K$$

where f_0 and f are the intensities of fluorescence of anthracene (A) with the concentration of quencher at zero and [Q] respectively, k is the experimental quenching constant, τ_0

[1] Bowen and Norton, *Trans Faraday Soc.*, 1939, **35**, 44.
[2] Bowen, Barnes, and Holliday, *Trans. Faraday Soc.*, 1947, **43**, 27.
[3] Bowen and Coates, *J.*, 1947, 105.
[4] Bowen and Metcalf, *Proc. Roy. Soc.*, 1951, *A*, **206**, 437.
[5] Bowen, *Trans. Faraday Soc.*, 1954, **50**, 97.
[6] Melhuish and Metcalf, *J.*, 1954, 976.

is the average life of the excited molecules in the absence of quencher, K is the equilibrium constant describing the formation of A*Q pairs:

$$A^* + Q \underset{k_2}{\overset{k_1}{\rightleftharpoons}} A^*Q \quad ; \quad K = \frac{k_1}{k_2} = \frac{[A^*Q]}{[A^*][Q]}$$

and k_3 is the first-order rate constant of the quenching step

$$A^*Q \xrightarrow{k_3} \text{products}$$

k_3 and K, unlike k_1 and k_2, are independent of diffusion and viscosity.[4, 6]

The Table gives data for the calculation of the experimental values of k for a variety of weak quenchers in four solvents from 20° to 60°, and for values of [Q] from zero to about $1/k$. The concentration of anthracene was that required for maximum fluorescence in each solvent, namely, light petroleum $3{\cdot}26 \times 10^{-4}$M, *cyclo*hexane $4{\cdot}0 \times 10^{-4}$M, benzene $1{\cdot}85 \times 10^{-4}$M, ethanol $4{\cdot}0 \times 10^{-4}$M.

The values of k_0 at 20° for the series Pr^nBr (1·50), $BrCH_2{\cdot}CO_2Et$ (1·76), $BrCH(CO_2Et)_2$ (14·3), and $BrCH(CN){\cdot}(CO_2Et)$(63) show clearly what the remaining values suggest, namely that electron-attracting substituents in alkyl halides enhance their quenching power. Further examples of this effect are Me_3CBr (0·61), Me_2CHBr (0·83), Pr^nBr (1·32), $Me{\cdot}CHBr{\cdot}CH_2Br$ ($2 \times 1{\cdot}8$), $CH_2Br{\cdot}CH_2Br$ ($2 \times 2{\cdot}6$); $CHCl_3$ ($3 \times 0{\cdot}03$), CCl_4 ($4 \times 0{\cdot}29$), and $CCl_3{\cdot}CO_2Et$ ($3 \times 0{\cdot}55$). In each series the compounds are listed in the order of the

$$k = k_0^{20}\{1 + a(T - 20) + b[Q]\}.$$

	Light petroleum			*cyclo*Hexane			Benzene			Ethanol		
Quencher	k_0^{20}	10^3a	b	k_0^{20}	10^3a	b	k_0^{20}	10^3a	b	k_0^{20}	10^3a	b
$CHCl_3$	0·095	—	0·036	—	—	—	0·085	−7	0·008	0·108	−2	0·046
CCl_4	1·17	19	−0·04	1·00	18	—	6·3	—	−0·095	10·9	13	−0·1
C_2Cl_6	1·58	19	+0·16	—	—	—	4·6	5	—	—	—	—
$CCl_3{\cdot}CO_2Et$	—	—	—	1·66	—	+0·72	—	—	—	—	—	—
p-$C_6H_4Cl_2$	0·37	−4	—	0·54	−6	−0·15	0·18	−1	—	0·38	−6	—
Me_3CBr	0·61	1	0·08	0·74	2	—	0·69	−1	0·0	—	—	—
Me_2CHBr	0·83	0	0·0	—	—	—	0·90	2	0·0	—	—	—
Pr^nBr	1·32	0	—	1·50	−2	—	1·25	−2	—	1·42	0	—
Bu^nBr	1·27	−2	0·0	—	—	—	—	—	—	—	—	—
*$BrCH_2{\cdot}CO_2Et$	—	—	—	1·76	—	0·14	—	—	—	—	—	—
*$BrCH(CO_2Et)_2$	—	—	—	14·3	—	−0·35	—	—	—	—	—	—
*$BrCH(CN){\cdot}CO_2Et$	—	—	—	63	—	—	—	—	—	—	—	—
PhBr	1·95	−3	0·03	2·15	−3	—	1·34	−3	—	2·12	−1	0·08
p-$Me{\cdot}C_6H_4Br$	2·33	−2	—	2·80	−4	—	1·65	−3	—	2·70	−1	—
p-$C_6H_4Br_2$	10·6	−5	—	10·6	−5	—	4·55	−2	0·0	8·9	−3	—
*p-$MeO{\cdot}C_6H_4Br$	—	—	—	3·85	—	−0·13	—	—	—	—	—	—
*p-$CO_2Me{\cdot}C_6H_4Br$	—	—	—	7·05	—	0·4	—	—	—	—	—	—
$Ph{\cdot}CH_2Br$	7·0	1	0·7	5·1	1	0·0	2·85	1	0·2	—	—	—
$MeCHBr{\cdot}CH_2Br$	3·69	−2	—	4·05	−4	—	2·97	−4	—	4·24	−1	—
$CH_2Br{\cdot}CH_2Br$	5·15	−4	0·0	—	—	—	3·72	−4	0·00	—	—	—
1 : 7-Dibromo-naphthalene	42	1	—	—	—	—	16·6	—	—	—	—	—
HI	161	—	0·6	—	—	—	49	—	1	—	—	—
MeI	21·9	−2	0·02	—	—	—	—	—	—	22·4	+3	—
EtI	23·3	0	—	18·9	0	—	16·4	−1	0·03	21·4	0	—
n-$C_5H_{11}I$	—	—	—	—	—	—	16·0	—	0·7	—	—	—
PhI	32·3	0	—	—	—	—	17·5	4	—	—	—	—

* We thank Mr. L. G. L. Ward for technical assistance with these measurements.

electron-attracting power of the substituents inferred from the dipole moments.[7] It appears that electrons move toward the quencher in the quenching process.

In the aromatic series the quenching constant of bromobenzene (2·15) is raised to

[7] Sutton, *Proc. Roy. Soc.*, 1931, *A*, **133**, 668.

7·05 by the strongly electron-attracting group *p*-CO_2Me. The other substituents have smaller effects which are not simply in the order of the bond moments.

Only carbon tetrachloride [2] and hexachloroethane have definite positive temperature coefficients of quenching, and quenching constants very sensitive to the solvent. Quenching by carbon tetrachloride has been treated as diffusion-limited,[2] but is unaffected by viscosity [1,6] and therefore cannot be diffusion-controlled. It is inferred that the quenching step in this case has an energy of activation which is sensitive to the nature of the solvent. The temperature-dependence of the other quenching constants is scarcely distinguishable from zero. In these cases there is thus no energy barrier to quenching which might be lowered by electron-attracting substituents. Such groups must enhance the probability of quenching in some other manner.

The lower quenching in benzene reflects the shorter lifetime τ_0 of anthracene in that solvent.

A more detailed analysis of the quenching processes [6] shows that the small dependence of k on [Q] is made up of a number of small terms which cannot be separated by experiment except in certain very favourable cases. We record this dependence to emphasise that it is very small but certainly detectable.

Experimental

Quenching was measured as described earlier.[6] The absorption of the exciting light (3650 Å) by the quenching substances was shown separately to be negligible.

The following substances were purified as recommended by Timmermans: [8] $CHCl_3$, CCl_4, C_2Cl_6, $C_6H_4Cl_2$, Me_3CBr, Me_2CHBr, Pr^nBr, Bu^nBr, PhBr, $Me{\cdot}C_6H_4Br$, $C_6H_4Br_2$, MeI, EtI, PhI.

The following were fractionally distilled: benzyl bromide, methyl trichloroacetate (b. p. 164—166°), ethyl bromoacetate ($d_4^{20} = 1{\cdot}5112$), ethyl bromomalonate (three fractions of identical quenching power), and ethyl bromocyanoacetate. The last decomposed slightly on distillation. The colourless fractions (presumed to be mixtures of ethyl bromocyanoacetate and ethyl cyanoacetate) were therefore analysed by adding them to acidified potassium iodide solution and titrating the iodine formed. Ethyl cyanoacetate does not quench.

Methyl *p*-bromobenzoate (m. p. 79·5—80·5°) and *p*-bromoanisole (m. p. 11·8—12·8°) were crystallised from methanol and fractionally frozen respectively.

Solutions of hydrogen iodide were estimated acidimetrically. *n*-Pentyl iodide was a sample described elsewhere.[9]

Benzene was treated with sulphuric acid to remove thiophen, which is a quencher. Light petroleum (b. p. 72—85°) and *cyclo*hexane were passed through a column of silica gel. The first liquid to come through is free from aromatic compounds as shown by the ultraviolet transmission.

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[8] Timmermans, "Physico-chemical Constants of Pure Organic Compounds," Elsevier, Amsterdam, 1950.
[9] Metcalf, *J.*, 1954, 2485.

85. *Diffusion Studies with Lysolecithin.*

By L. Saunders and I. L. Thomas.

A method for preparing crystalline lysolecithin is described. This material gave clear sols in water and so diffusion coefficients could be determined by the Gouy method. Measurements showed that the diffusion coefficient (D) was independent of sol concentration in the range studied. The low value of D and the regularity of the interference patterns indicated the presence of large, uniform micelles in the sols. The presence of calcium chloride did not affect either D or the viscosity of a sol.

The phosphatides are important constituents of cell membranes and studies of the physical properties of their sols in water should contribute to our knowledge of formation of cell membranes. We now give details of a method for preparing crystalline lysolecithin. Diffusion and viscosity measurements have been carried out with its sols over a limited concentration range. The effect of calcium chloride on diffusion and viscosity of a lysolecithin sol has also been studied, since this salt has an important effect on the stability of lecithin sols.

The viscosity of the lysolecithin sols varied with the viscometer used, indicating that the sols exhibited non-Newtonian flow. Changes in viscosity were followed by observing the times required for a fixed volume of the sols to pass through a particular viscometer.

Experimental

The diffusion was measured across a free boundary by using a Gouy diffusiometer described previously.[1,2]

Materials.—Lysolecithin. This was prepared by a method based on that of Hanahan, Rodbell, and Turner.[3] The yolks of 24 eggs were broken and stirred for a few minutes with 1 l. of acetone. The solution was then filtered, and the residue washed with fresh acetone. This process was repeated once. To the residue were added 300 ml. of warm ethyl alcohol. After being stirred, the alcoholic solution was decanted off and this process was repeated four times. The alcoholic solution was then evaporated under reduced pressure to dryness, the temperature being kept below 55°. The dry extract was dissolved in the minimum quantity of warm ether and the solution was added, with stirring, to a sufficient quantity of acetone to precipitate all the phosphatides. The precipitate was centrifuged off and dissolved in 500 ml. of ethyl alcohol. Alumina was added to the solution until it gave no coloration on heating with ninhydrin solution, indicating the complete removal of cephalins and other phosphatides containing primary amino-groups. The alcoholic solution was filtered and evaporated to dryness to give a residue of lecithin containing some lysolecithin. This was dissolved in ether so as to give a 1% solution, which was not completely clear owing to the insolubility of lysolecithin in ether. To the ethereal solution was added 10 mg. of Russell viper venom, which had been dissolved in 10 ml. of water. The mixture was shaken and kept for 1 hr. at room temperature. Most of the supernatant liquid was decanted off, leaving a gelatinous precipitate of lysolecithin: treatment of this with acetone caused flocculation, so that the remaining supernatant liquid was easily decanted off. The solid was then dissolved in the minimum amount of warm chloroform, and thence precipitated by addition of excess of ether. The precipitate was separated by decantation, and the process repeated three times. The lysolecithin was then dissolved in warm ethyl alcohol so as to give about a 20% solution. The warm solution was centrifuged to remove the residue from the venom present as a suspended solid and the lysolecithin was then allowed to crystallise from the alcoholic solution at 0°. This crystallisation was repeated three times (Found: N, 2·8; P, 5·7%).

Calcium chloride. "AnalaR" reagent was used.

Preparation of Sols.—Lysolecithin sol. The lysolecithin was dissolved in a small volume of distilled water, with the aid of very gentle warming. The sol was then passed over a bed of

[1] Saunders, *J.*, 1953, 519.
[2] Brudney and Saunders, *J.*, 1955, 2916.
[3] Hanahan, Rodbell, and Turner, *J. Biol. Chem.*, 1954, **206**, 431.

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mixed Amberlite ion-exchange resins IR-120(H) and IRA-400(OH) to remove any traces of non-colloidal electrolyte present. The resins were then washed with small successive portions of distilled water and the sol was finally made up to volume. The specific conductivity of a 1% sol was 160,000 mhos/cm. Concentrations are expressed as % (w/v).

Lysolecithin sol containing calcium chloride. A sol of lysolecithin in water was prepared as above, except that the concentration of the sol was twice that required in the final sol. To this was added an equal volume of calcium chloride solution of twice the concentration required in the final sol.

Results.—In Table 1 are given the results obtained from three Gouy patterns observed when a solution of 1·1% lysolecithin diffused into water. These show the consistency of C_t.

Effect of Temperature on D.—The integral diffusion coefficient for a 1·4% sol of lysolecithin at 30° was $6{\cdot}72_2 \times 10^{-7}$ cm.^{2} sec.$^{-1}$.

Effect of Calcium Chloride.—Sols were prepared containing 1·2% of lysolecithin and varying concentrations of calcium chloride as shown in Table 3. Boundaries were then formed in the diffusion cell, between these sols and solutions containing the same concentrations of calcium chloride as the sols but without the lysolecithin.

TABLE 1. *Integral diffusion coefficient for a 1·1% lysolecithin sol.*

$j_m = 77{\cdot}0$ (the symbols are defined in *J.*, 1953, 519).

	t = 19,140 sec.		t = 24,600 sec.		t = 27,540 sec.	
j	γ	C_t	γ	C_t	γ	C_t
1	1·3507	1·496	1·1924	1·320	1·1262	1·247
2	1·3003	1·495	1·1472	1·319	1·0842	1·246
3	1·2561	1·492	1·1097	1·318	1·0485	1·245
4	1·2178	1·494	1·0737	1·317	1·0146	1·245
5	1·1799	1·492	1·0414	1·317	0·9850	1·245
6	1·1462	1·494	1·0105	1·317	0·9553	1·243
7	1·1130	1·494	0·9820	1·318	0·9286	1·246
8	1·0811	1·493	0·9548	1·319	0·9024	1·246
9	1·0508	1·493	0·9287	1·319	0·8772	1·246
10	1·0222	1·492	0·9037	1·319	0·8531	1·245
s		0·0014		0·0010		0·0014
10^7D		$6{\cdot}57_2$		$6{\cdot}56_4$		$6{\cdot}57_8$

D (Average for 5 patterns) $= 6{\cdot}57 \times 10^{-7}$.

(s is the standard deviation of each column of C_t values. D is the diffusion coefficient in cm.^{2} sec.$^{-1}$.)

DISCUSSION

The low value obtained for the diffusion coefficient of lysolecithin indicates that in water it exists in the form of large micelles. The regular nature of the Gouy patterns obtained shows that only one diffusing component is present, *i.e.*, the micelles must be of fairly uniform size.

The micelles being assumed spherical, the volume of a single micelle can be calculated by using the Stokes–Einstein equation from which the molar volume of a micelle was found to be $1{\cdot}289 \times 10^5$ c.c. corresponding to a volume of $2{\cdot}15 \times 10^5$ Å^3 per molecule.

In order to estimate the molar volume of monomeric lysolecithin, the density of the solid was determined by a flotation technique with di-iodomethane–benzene. This gave a value of 1·095 g. ml.$^{-1}$, corresponding to a molar volume of 472 ml. Division of the micellar volume by this gave a value of 273 as the mean number of molecules in a micelle.

Statistical Analysis of Results.—When the results of Table 2 are plotted as a graph showing the variation of diffusion coefficient with concentration, some scatter is observed as is expected with a colloid. A summary of a statistical analysis of these results and those of Table 3 is given below.

(1) *Data of Table* 2. In order to assess the variation of the diffusion coefficient D with concentration c, the correlation coefficient r was calculated. In Table 2 the values of D given are in fact the means of four or more Gouy patterns analysed for each concentration. In the statistical calculations all the individual values of D for each Gouy pattern have been

included, except for the first two results in the table, where an extrapolation procedure had to be adopted; in these cases the single extrapolated values of D were taken, thus giving these two results less weight than the others. There were 39 degrees in the

TABLE 2. *Diffusion coefficients and viscosities of lysolecithin sols.*

Concn. of lysolecithin (w/v %)	Integral diffusion coeff. D at 25° (cm.^{2} sec.$^{-1}$)	Time (sec.) required for solution to pass through viscometer at 25°
0·88	$6{\cdot}55_5$ *	1123
0·94	$6{\cdot}55_0$ *	1125
1·02	$6{\cdot}62_8$	1127
1·10	$6{\cdot}57_3$	1131
1·20	$6{\cdot}50_1$	1132
1·30	$6{\cdot}59_7$	1134
1·40	$6{\cdot}41_8$	1137
1·58	$6{\cdot}36_0$	1143
1·72	$6{\cdot}55_1$	1147
1·87	$6{\cdot}57_5$	1152

* Indicates an extrapolated value. In these experiments it was found that D decreased with time, and the true diffusion coefficient was obtained by plotting D against $1/t$ and extrapolating to $1/t = 0$.[1]

No results could be obtained with sols of concentration below 0·88% since the density differences between the sols and water were too small for stable boundaries to be formed.

TABLE 3.

$CaCl_2$ concn. (M)	10^{-1}	10^{-2}	10^{-3}	10^{-4}	10^{-5}	10^{-6}
10^7D	$6{\cdot}42_3$	$6{\cdot}58_0$	$6{\cdot}45_0$	$6{\cdot}59_7$	$6{\cdot}37_1$	$6{\cdot}34_0$
Viscosity relative to pure lysolecithin sol	1·00	0·99	0·99	0·99	0·99	1·00

calculation of the correlation coefficient of D with c, and its value was $r = -0{\cdot}26$. The theoretical value of r for the 0·95 probability level is 0·35,[4] and therefore, since the calculated value is appreciably less in magnitude than the theoretical one, the correlation is not significant, *i.e.*, there is no real variation of D with c.

This result being accepted, the variance of the diffusion coefficient values about their mean was estimated as $6{\cdot}464 \times 10^{-17}$ with 39 degrees of freedom. This corresponded to a standard deviation of $0{\cdot}08 \times 10^{-7}$. From this, limits of error of a diffusion coefficient of lysolecithin determined from five Gouy patterns were estimated as $\pm 0{\cdot}097 \times 10^{-7}$ at the 0·99 probability level. The mean value of D was $6{\cdot}544 \times 10^{-7}$ and so these limits as a percentage of the mean are $\pm 1{\cdot}48$.

(2) *Data of Table* 3. A correlation coefficient for the variation of D with calcium chloride concentration was calculated as $-0{\cdot}117$, with five degrees of freedom. The theoretical value at the 0·95 probability level is 0·754.[4] Since the observed value is much smaller in magnitude than this it is concluded that the diffusion coefficient is independent of calcium chloride concentration. A t-test showed that the mean value of D in the presence of calcium chloride does not differ significantly from the mean value for the pure sols.

The conclusion that both D and the relative viscosity of a lysolecithin sol are unaffected by the presence of calcium chloride was unexpected in view of the marked effect of calcium salts on lecithin sols.[5] It had been expected that bonding between the calcium ions and the phosphate groups of the lysolecithin would have caused a reduction in the rate of diffusion and an increase in relative viscosity.

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SCHOOL OF PHARMACY, LONDON, W.C.1. [*Received, July 8th*, 1957.]

[4] Saunders and Fleming, "Mathematics and Statistics," p. 162, Pharmaceutical Press, London, 1957.
[5] Elworthy and Saunders, *J.*, 1957, 330.

86. *The Visible and Ultraviolet Spectra of Some Platinous Ammines.*

By J. Chatt, G. A. Gamlen, and L. E. Orgel.

The visible and ultraviolet spectra of the ions $[Pt(NH_3)_nCl_{4-n}]^{(n-2)+}$ for $n = 0$—4 have been measured and tentatively interpreted in terms of the orbital energy diagram for *d* electrons on the platinous ion. The spread of *d*-orbital energies is greater (30,000—40,000 cm.$^{-1}$) than usual, and appears to be due to electrostatic and σ-bonding effects rather than to π-bonding. The chemical implications of this fact are discussed.

The spectra of octahedral complexes of the transition metals have often been investigated theoretically and practically. The nature of the weak, long-wavelength absorption bands is now understood fairly well and their detailed assignments to transitions within the d^n configuration of the metal ion have been made for many compounds.[1] The corresponding problem for planar complexes is more difficult since the effect of the ligands on the energies of the different *d*-orbitals is much more complicated. We now study in detail the spectra of a series of platinous ammines and suggest some assignments. These are provisional in that, while they give the best overall interpretation of the available experimental data, other assignments are not excluded.

Table 1. *Frequency of maxima* ($\nu_{max.}$),* *maximum extinction coefficients* ($\varepsilon_{max.}$) *and half-widths of the bands* ($\nu_{\frac{1}{2}}$) * *in the absorption spectra of* K_2PtCl_4, *and the derived platinous ammines. The solvent was water, except as indicated.*

	$\nu_{max.}$	$\varepsilon_{max.}$	$\nu_{\frac{1}{2}}$	$\nu_{max.}$	$\varepsilon_{max.}$	$\nu_{\frac{1}{2}}$	$\nu_{max.}$	$\varepsilon_{max.}$	$\nu_{\frac{1}{2}}$
K_2PtCl_4	1·77	2·6	0·10	2·10	15·0	0·203	2·55	59	0·14
$K[NH_3PtCl_3]$	2·07	2·8	0·14	2·41	19·8	0·24	2·89	118	0·15
trans-$(NH_3)_2PtCl_2$	—	—	—	2·68	21·4	0·25	3·17	60	0·17
trans-$[\{(C_5H_{11})_2NH\}_2PtCl_2]$ †	2·26	2·2	0·22	2·64	21·8	0·20	3·12	67·4	—
cis-$[(NH_3)_2PtCl_2]$	2·40	3·2	0·16	2·73	23	0·23	3·31	128	0·22
$[(NH_3)_3PtCl]_2SO_4$	—	—	—	3·10	65	0·27	3·60	80	0·16
$[(NH_3)_4Pt]Cl_2$	—	—	—	3·48	36	0·23	—	—	—
Suggested assignment ...	triplet $d_{xy} \rightarrow d_{x^2-y^2}$			triplet d_{yz}, $d_{zx} \rightarrow d_{x^2-y^2}$			singlet $d_{xy} \rightarrow d_{x^2-y^2}$		

	$\nu_{max.}$	$\varepsilon_{max.}$	$\nu_{\frac{1}{2}}$	$\nu_{max.}$	$\varepsilon_{max.}$	$\nu_{\frac{1}{2}}$	$\nu_{max.}$	$\varepsilon_{max.}$
K_2PtCl_4	3·02	64	0·17	3·79	250	0·03	4·6	9580
$K[NH_3PtCl_3]$	3·33	74	0·21	—	—	—	>4·75	>6000
trans-$(NH_3)_2PtCl_2$	3·67	75	0·25	—	—	—	4·6	2110
trans-$[\{(C_5H_{11})_2NH\}_2PtCl_2]$ †	3·71	97·2	—	—	—	—	>4·65	>4000
cis-$[(NH_3)_2PtCl_2]$	3·72	68·5	0·21	—	—	—	>4·76	>4500
$[(NH_3)_3PtCl]_2SO_4$	3·97	233	0·32	—	—	—	>4·8	>6000
$[(NH_3)_4Pt]Cl_2$	—	—	—	—	—	—	>4·87	>3000
Suggested assignment ...	singlet d_{zz}, $d_{yz} \rightarrow d_{x^2-y^2}$						$d \rightarrow p$	

* Frequencies are in 10^4 cm.$^{-1}$. † In ethanol.

Spectra.—The spectra of the complexes $[Pt(NH_3)_nCl_{4-n}]^{(n-2)+}$ for $n = 0$—4, measured in aqueous solution, are presented in Figs. 1—3. The spectrum of *trans*-$[\{(n\text{-}C_5H_{11})_2NH\}_2PtCl_2]$ has been included in Fig. 2 since the long-wavelength region of the spectrum of *trans*-$[Pt(NH_3)_2Cl_2]$ could not be measured accurately on account of the low solubility of the compound. In Fig. 4 we compare the spectra of *trans*-$[\{(n\text{-}C_5H_{11})_2NH\}_2PtCl_2]$ in ethanol and in hexane.

We analysed the measured spectra assuming that they can be represented as sums of Gaussian absorption bands. The results of this analysis are given in Table 1 and the variations of the positions of the various bands with *n* in Fig. 5.

Interpretation.—The transformation properties of the *d*, *s*, and *p* orbitals of the central

[1] (*a*) Jørgensen, Report of the 10th Solvay Conference in Chemistry, Brussels, 1956; (*b*) Orgel, *J. Chem. Phys.*, 1955, **23**, 1004.

FIG. 1. *Ultraviolet spectra of* $K[NH_3PtCl_3]$ *(solid line) and* K_2PtCl_4 *(broken line).*

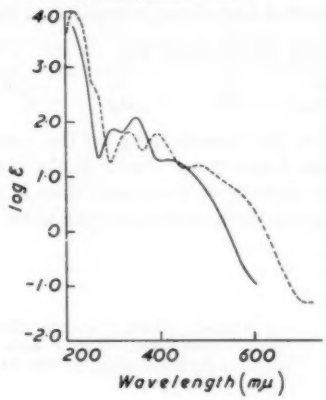


FIG. 2. *Ultraviolet spectra of* cis-$[(NH_3)_2PtCl_2]$ *(solid line),* trans-$[(NH_3)_2PtCl_2]$ *(dotted line), and* trans-$[\{(n\text{-}C_5H_{11})_2NH\}_2PtCl_2]$ *(broken line). The last plot, taken in ethanol, has been lowered by* 0·5 *log unit.*

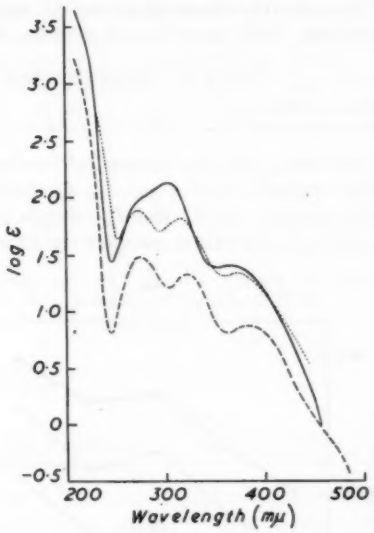


FIG. 3. *Ultraviolet spectra of* $[(NH_3)_4Pt]Cl_2,H_2O$ *(solid line) and* $[(NH_3)_3PtCl]_2SO_4$ *(broken line).*

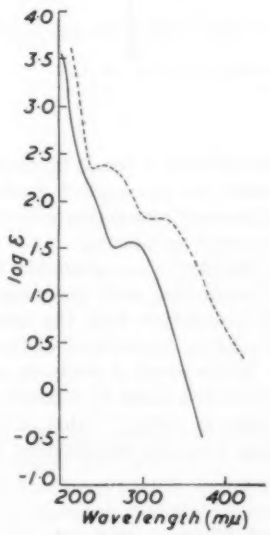
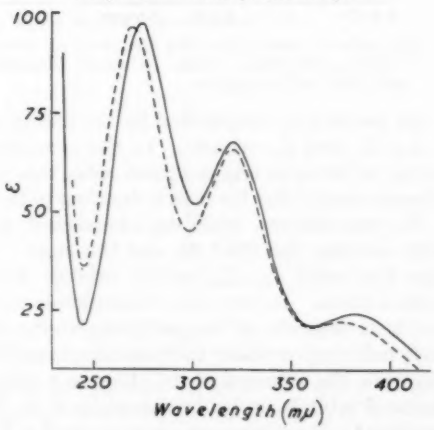


FIG. 4. *Ultraviolet spectrum of* trans $[\{(C_5H_{11})_2NH\}_2PtCl_2]$ *in ethanol (solid line) and* n*-hexane (broken line).*



metal ion in the group D_{4h} of a symmetrical planar MX_4 complex are given in Table 2. The choice of axes is illustrated in Fig. 6.

Ligand-field theory shows that the $d_{x^2-y^2}$ orbital, or more correctly the orbital which is largely $d_{x^2-y^2}$ in character, is much less stable than the other d orbitals, since it points directly at the ligands and is made less stable by them.[2] The order of stability within the remaining group of d-orbitals cannot be settled theoretically.

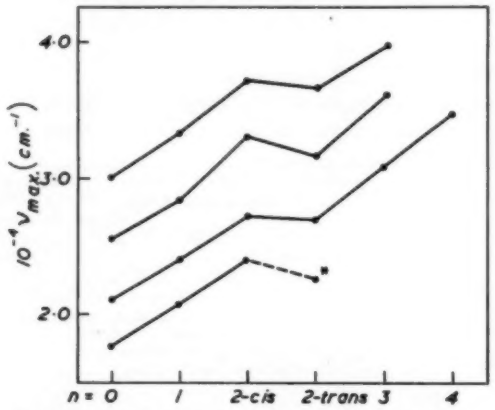
Electrostatic effects alone would make the d_{xz} and d_{yz} orbitals more stable than the d_{xy} orbital. This may be seen most easily by supposing that the planar complex has been

TABLE 2. *Symmetry classification of orbitals for the group D_{4h}.*

Atomic orbital	s	p_x, p_y	p_z	d_{z^2}	$d_{x^2-y^2}$	d_{xy}	d_{xz}, d_{yz}
Symmetry type	A_{1g}	E_u	A_{2u}	A_{1g}	B_{1g}	B_{2g}	E_g

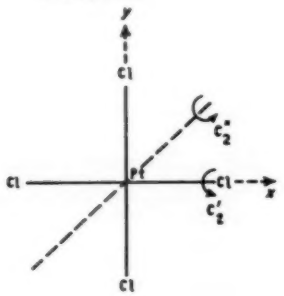
derived from a regular octahedral one by the removal of the ligands lying on the z axis. In the original complex the d_{xz}, d_{yz}, and d_{xy} orbitals are degenerate. Since in the octahedral complex the d_{xz} and d_{yz} orbitals are closer to the ligands on the z axis than is the d_{xy} orbital, in the planar complex the former orbitals must be more stable than the latter.

FIG. 5. *Values of $\nu_{max.}$ for the spectra of $[Pt(NH_3)_nCl_{4-n}]^{(n-2)+}$, where $n = 0$—4.*



* This point is taken from the spectrum of *trans*-$[\{(C_5H_{11})_2NH\}_2PtCl_2]$ which is almost identical with that of the ammine.

FIG. 6. *Choice of axes for planar complexes. The z axis is perpendicular to the molecular plane.*



The problem is complicated by the ability of some ligands to form π bonds involving the d_{xy}, d_{xz}, and d_{yz} orbitals. In the complexes now discussed, we can neglect double-bonding to the ammonia molecules, since this is only possible through interaction with the hydrogen atoms,[3] but the double-bonding to the chloride ions cannot be ignored.

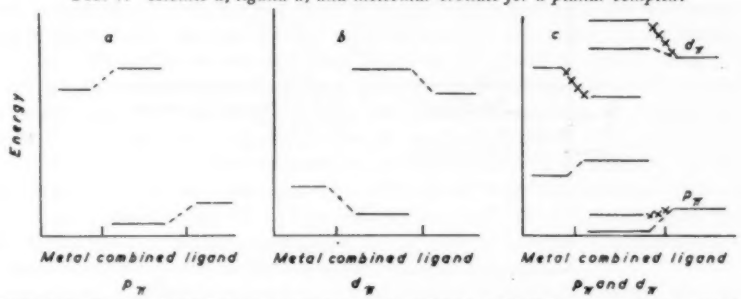
The chloride ion, with the closed-shell structure . . . $(3s)^2(3p)^6$, has available for double-bonding the filled $3p$ and the empty $3d$ orbitals. Interaction with the former makes the metal d_{xy}, d_{xz}, and d_{yz} orbitals less stable, while interaction with the latter stabilises them. In any given transition-metal complex the relative importance of these two effects depends on the electronegativity of the metal. If the metal d electrons are loosely held they are likely to be stabilised, and if tightly held made less stable by π-bonding. Thus while the influence of the chlorine p orbitals must be large in $[PtCl_6]^{2-}$, that of the chlorine d orbitals probably outweighs it in $[PtCl_4]^{2-}$, leading to a net stabilisation by π-bonding.[4] These relations are illustrated in Fig. 7.

[2] Orgel, *J.*, 1952, 4756.
[3] Chatt, Duncanson, and Venanzi, *J.*, 1955, 4461.
[4] (*a*) Chatt, Duncanson, and Venanzi, *J.*, 1956, 2712; (*b*) Chatt and Wilkins, *J.*, 1956, 525.

In the case of the $[PtCl_4]^{2-}$ ion, the metal d_{xz} and d_{yz} orbitals can each interact with the two d_π orbitals on the chloride ions. The d_{xy} orbitals, however, can interact with four chlorine d_π orbitals, and so should be stabilised a little more, as shown in Fig. 8. We do not believe that this effect is very large, certainly not large enough to disturb the order of levels determined by the electrostatic effect.

The d_{z^2} orbital is much more difficult to place on an energy scale for several reasons. First, simple electrostatic calculations do not lead to unambiguous conclusions, for the order of the d_{xy}, d_{xz}, and d_{yz} orbitals on the one hand and the d_{z^2} orbital on the other depends critically on the details of the model chosen. Secondly, molecular-orbital theory shows that the d_{z^2} and s orbitals can become mixed together in a planar complex. One combin-

FIG. 7. *Atomic d, ligand π, and molecular orbitals for a planar complex.*



a, Only ligand p_π orbitals included; *b*, only ligand d_π orbitals included; *c*, ligand p_π and d_π orbitals included for high electronegativity (— — —) or low electronegativity (× × ×) of the metal orbitals.

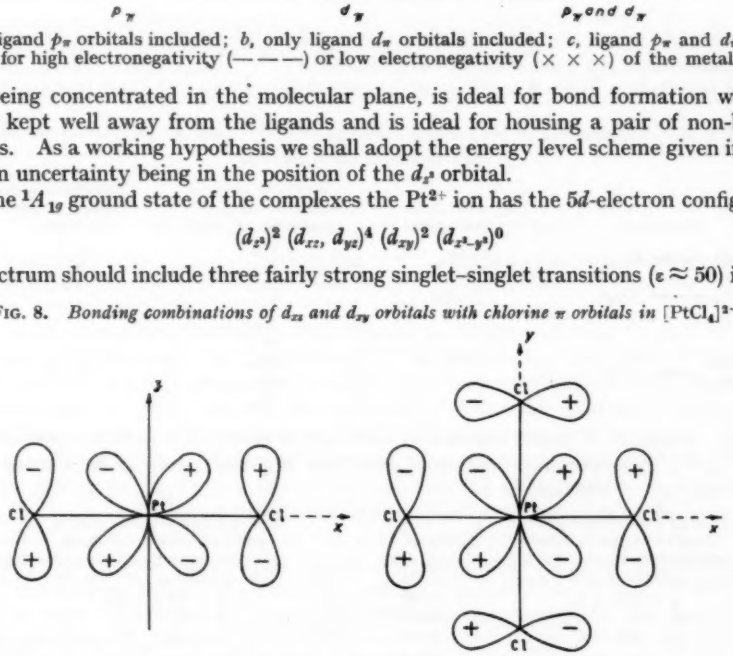
ation, being concentrated in the molecular plane, is ideal for bond formation while the other is kept well away from the ligands and is ideal for housing a pair of non-bonding electrons. As a working hypothesis we shall adopt the energy level scheme given in Fig. 9, the main uncertainty being in the position of the d_{z^2} orbital.

In the $^1A_{1g}$ ground state of the complexes the Pt^{2+} ion has the $5d$-electron configuration

$$(d_{z^2})^2\ (d_{xz},\ d_{yz})^4\ (d_{xy})^2\ (d_{x^2-y^2})^0$$

The spectrum should include three fairly strong singlet–singlet transitions ($\varepsilon \approx 50$) in which

FIG. 8. *Bonding combinations of d_{xz} and d_{xy} orbitals with chlorine π orbitals in* $[PtCl_4]^{2-}$.



an electron is removed from one of the filled d orbitals and placed in the $5d_{x^2-y^2}$ orbital and three or four somewhat weaker transitions to the corresponding triplets. The situation differs from that in the first transition series, because the spin–orbit coupling is so strong for platinum that the intensity of the singlet–triplet transitions may approach that for the spin-allowed transitions (the approximation of Russell–Saunders coupling is not really

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valid, and the classification of states into singlets and triplets is only meant in an approximate sense). In the first two columns of Table 3 we classify the states of the d^8 configuration to which one-electron transitions are possible. By $d_{xy} \longrightarrow d_{x^2-y^2}$ we denote the sub-configuration arising from the ground-state configuration by the promotion of an electron from the d_{xy} to the $d_{x^2-y^2}$ orbital, etc. The ^3E_g state is split by spin–orbit interaction and could conceivably give rise to two absorption bands.

The energies of the excited states relative to the ground state do not correspond directly to the separations in Fig. 9, for the latter do not allow for the changes in the *d*-electron repulsion energy which accompany excitation. This quantity, together with

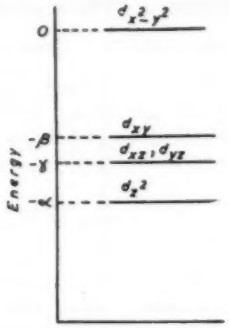

FIG. 9. *Provisional energy-level scheme for d orbitals in* $[PtCl_4]^{2-}$.

the energies of the various relevant states, was calculated in terms of Slater–Condon or Racah parameters by methods already described.[5,6] The various energy terms are collected together in Table 4 together with some rough guesses at their numerical values.

TABLE 3. *Symmetries of the excited states of* $[PtCl_4]^{2-}$ *and of the vibrations making transitions to them allowed.*

Transition	Symmetry of upper state	Vibration making singlet–singlet transition allowed	Polarisation of singlet–singlet transition
$d_{z^2} \longrightarrow d_{x^2-y^2}$	$^{1,3}B_{1g}$	B_{2u}	z
		E_u	x, y
$d_{xy} \longrightarrow d_{x^2-y^2}$	$^{1,3}A_{2g}$	A_{1u}	z
		E_u	x, y
d_{xz} / $d_{yz} \longrightarrow d_{x^2-y^2}$	$^{1,3}E$	E_u	z
		A_{1u}, A_{2u}, B_{1u}, B_{2u}	x, y

TABLE 4. *Energies of states obtained by one-electron transitions from the ground state of* $[PtCl_4]^{2-}$. *Configurative interaction has been neglected, and we have assumed* $B = 750\ cm.^{-1}$, $C = 3000\ cm.^{-1}$.

State	Energy relative to ground state in terms of Racah parameters [5,6] and crystal-field splittings (see Fig. 9)	Estimate of Racah term ($cm.^{-1}$)	State	Energy relative to ground state in terms of Racah parameters [5,6] and crystal-field splittings (see Fig. 9)	Estimate of Racah term ($cm.^{-1}$)
$^1B_{1g}$	$\alpha - 4B - C$	−6000	$^3B_{1g}$	$\alpha - 12B - 3C$	−18,000
$^1A_{2g}$	$\beta - C$	−3000	$^3A_{2g}$	$\beta - 3C$	−9000
^1E_g	$\gamma - 3B - C$	−5250	^3E_g	$\gamma - 9B - 3C$	−15,750

The additional term has the effect of complicating the assignments, since the upper singlet states corresponding to the $d_{z^2} \longrightarrow d_{x^2-y^2}$, and $d_{xz}, d_{yz} \longrightarrow d_{x^2-y^2}$ transitions are lowered relative to that of the $d_{xy} \longrightarrow d_{x^2-y^2}$ transition by 2000—3000 cm.$^{-1}$. This again raises

[5] Orgel, *J. Chem. Phys.*, 1955, **23**, 1819.
[6] Griffith, *J. Inorg. Nuclear Chem.*, 1956, **2**, 1.

doubts about the order of the $^1A_{2g}$ and ^1E_g upper states which, together with our uncertainty of the position of the $^1B_{1g}$ state, prevent our making any firm predictions on the basis of purely theoretical considerations. To make any further progress we have to consider the experimental data in greater detail.

The spectrum of $[PtCl_4]^{2-}$ beyond 300 mμ consists of four bands. The two at 331 mμ and 392 mμ ($3{\cdot}02 \times 10^4$ and $2{\cdot}55 \times 10^4$ cm.$^{-1}$ respectively) are clearly due to singlet–singlet transitions, since they have just the expected intensity. The weak band at 565 mμ ($1{\cdot}77 \times 10^4$ cm.$^{-1}$) is equally clearly due to a singlet–triplet transition, for the first excited state must be a triplet. The intensity of this transition is, if anything, a little small for a spin-forbidden band in a platinum complex.

The assignment of the band at 476 mμ ($2{\cdot}10 \times 10^4$ cm.$^{-1}$), which has intermediate intensity, is less clear. We believe that it is another triplet, for the following reasons. First, each band at 331 mμ and 392 mμ must have a corresponding triplet band at longer wavelengths. We can see no trace of weak bands except at 476 mμ and 565 mμ. Secondly, the energy separations between the 331 mμ and 476 mμ bands and between the 392 mμ and 565 mμ bands seem very reasonable if they are corresponding pairs of singlets and triplets (see Table 4). Finally the longest-wavelength band of $[Pt(NH_3)_4]^{2+}$, which must correspond to a transition to a triplet upper state, is even more intense than that of the 476 mμ band, showing that the moderate intensity of the band is not inconsistent with our assignment. These arguments are all rather indirect, so that the assignment may have to be reversed in the light of further experiments on related compounds, particularly if our guess at the position of the d_{z^2} orbital proves incorrect.

In crystals of K_2PtCl_4 there are two fairly strong absorption bands, one at 375 mμ which has its transition vector in the plane of the molecule and the other at 340 mμ with its transition vector perpendicular to that plane.[7] There is a much weaker transition at 500 mμ which is not polarised. It seems natural to associate these bands with the solution bands at 392 mμ, 331 mμ, and 476 mμ, respectively. In order to interpret these polarisation data we have to discuss the mechanism by which the forbidden g–g electronic transitions are made allowed.

TABLE 5. *Symmetry of* $[PtCl_4]^{2-}$ *vibrations.*

Type of vibration	Stretching			Bending in plane		Bending out of plane	
Symmetry type	A_{1g}	B_{1g}	E_u	B_{2g}	E_u	A_{2u}	B_{2u}

The usual mechanism by which g–g transitions become allowed in molecules is by vibrational perturbation.[8] In Table 5 we list the symmetry characters of the proper vibrations of the $[PtCl_4]^{2-}$ group, and in Table 3 the way in which the different electronic transitions may be made allowed by vibrations. Now the electronic energy of the $[PtCl_4]^{2-}$ ion is particularly sensitive to the Pt–Cl distances, and hence the stretching frequencies should play a dominant rôle in making the transitions allowed. Since the only u stretching frequency has the symmetry class E_u, transitions to A_{2g} or B_{1g} states should be polarised parallel, and transitions to the E_g state perpendicular, to the molecular plane. This suggests that the band at 375 mμ has an upper state of A_{2g} or B_{1g} symmetry, while the upper state of the 340 mμ band has E_g symmetry. The most probable assignment of the singlets is thus 375 mμ $\approx d_{xy} \longrightarrow d_{x^2-y^2}$ and 340 mμ $\approx d_{xz},d_{yz} \longrightarrow d_{x^2-y^2}$. If this is so, the triplets at 565 mμ and 476 mμ correspond to the same pair of sub-configurations.

In the series of compounds $[Pt(NH_3)_nCl_{4-n}]^{(n-2)+}$ it is possible to recognise a steady evolution of the position of the absorption bands with increasing n, as shown in Fig. 5. The regularities indicated in the Figure allow us to take over our tentative assignments

[7] Yamada, *J. Amer. Chem. Soc.*, 1951, **73**, 1182.
[8] Moffitt and Ballhausen, *Ann. Rev. Phys. Chem.*, 1956, **7**, 107.

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from $[PtCl_4]^{2-}$ to the whole group of ions. While the group-theoretical classification will be different in the lower symmetry groups of many of the molecules, the character of the orbitals involved must be only slightly modified. It follows that the designations such as $d_{xy} \longrightarrow d_{x^2-y^2}$ retain their original meanings.

The establishment of a simple correspondence between the bands of $[PtCl_4]^{2-}$ and $[Pt(NH_3)_2Cl_2]$ allows us further to test our assignments. By working with $[\{(n\text{-}C_5H_{11})_2NH\}_2PtCl_2]$, which has a spectrum closely similar to that of the simple ammine, we can study the effect of different solvents on the absorption bands. The band at 321 mμ is unaffected by the change from hexane to ethanol as solvent (Fig. 4), while those at about 270 mμ and 374 mμ are definitely shifted to longer wavelengths.

The effect of a polar solvent can be understood if it is realised that the positive charge on the Pt^{II} ion will lead to an orientation of the dipole moment of the solvent so that the negative end is close to the molecular plane. This type of residual interaction can even lead to the formation of compounds as Harris, Nyholm, and Stephenson [9] showed in the case of [Pd(diarsine)$_2$I$_2$]. The presence of very weakly attracted dipolar molecules of this sort makes the d_{z^2}, d_{xz}, and d_{yz} orbitals less stable relative to the d_{xy} and $d_{x^2-y^2}$ orbitals, while affecting the latter pair equally. Thus the $d_{z^2} \longrightarrow d_{x^2-y^2}$ and $d_{xz},d_{yz} \longrightarrow d_{x^2-y^2}$ transitions should show a red shift in a polar solvent, while the $d_{xy} \longrightarrow d_{x^2-y^2}$ transitions should be unchanged.[10] Thus our assignment does predict correctly the red-shift of the 270 mμ and 374 mμ bands and the unchanged position of the 321 mμ band when ethanol is used instead of hexane as a solvent.

Finally we discuss the magnitude of the ligand-field effects. In octahedral complexes of bivalent transition-metal ions of the first series the energy difference between the stable t_{2g} and the less stable e_g orbitals is about 10,000 cm.$^{-1}$. In corresponding complexes of the third transition series somewhat larger values of about 15,000—20,000 cm.$^{-1}$ would be expected. In the complexes which we have studied the spread of the *d*-orbital energies is much greater, perhaps 30,000—40,000 cm.$^{-1}$. Planar Cu^{2+} complexes also have *d*-orbital energy splittings greater than those for similar octahedral complexes. An interpretation of this fact has been suggested.[11]

Our results enable us to make a number of deductions of chemical interest about the electronic structure of platinous and related complexes. First, the fact that there is no sign of a splitting of the $d_{xz},d_{yz} \longrightarrow d_{x^2-y^2}$ transition in *trans*-$[PtCl_2(NH_3)_2]$ suggests strongly that the energy of the $d_{x^2-y^2}$ orbital is much more sensitive to the nature of the ligands than are those of the d_{xz} and d_{yz} orbitals. (One cannot exclude the possibility that the effects of the Cl^- and NH_3 on the d_{xz} or d_{yz} orbitals are large but equal; however this seems improbable in view of the general tendency of NH_3 to produce much greater splittings than does Cl^-.) This implies that electrostatic and σ-bond effects are more important than π-bonding. This conclusion agrees with much qualitative physical and chemical evidence on the nature of the bonding in platinous and related complexes.[3,12] While we cannot separate rigorously the electrostatic from the σ-bonding effects on the basis of optical spectra, on general grounds we believe the σ-bonding to be important in platinous compounds and responsible for a significant part of the *d*-orbital splitting.

Secondly, the ligand-field splitting is much greater for NH_3 than it is for Cl^-. This is the order found for compounds of the first transition series and also for Rh^{3+} and Ir^{3+} complexes. Furthermore, the observed crystal-field splittings for Br^- are always somewhat smaller than those for Cl^- in corresponding compounds. It seems, therefore, that small ligand-field splittings are characteristic of the heavier halogen ions in all their complexes.

If this generalisation is reliable it raises a very important question. Is it true that chloride complexes tend to be more " covalent " than hydrates or ammines in the sense

[9] Harris, Nyholm, and Stephenson, *Nature*, 1956, **177**, 1127.
[10] McGarvey, *J. Phys. Chem.*, 1956, **60**, 71.
[11] Orgel, Report of the 10th Solvay Conference in Chemistry, Brussels, 1956.
[12] Ahrland and Chatt, *J.*, 1957, 1379.

implied by Pauling,[13] *i.e.*, do they tend to have low spin values? There does not seem to be any experimental evidence that this is so. Chloride complexes of the second and third sub-group elements such as $[IrCl_6]^{2-}$ have low spin values, but so also do the corresponding hydrates, etc. No significant comparisons have been made for the complexes of the first series in solids or in solution. The magnetic susceptibilities of binary halides are certainly unusual, but in all the cases studied in detail this is due to antiferromagnetic interactions rather than to spin pairing on a single ion. While it is possible that the halides of certain ions will be found to have low spin although the corresponding hydrates have high spin, for example, if delocalisation is much more extensive in the former than in the latter, in the absence of experimental evidence this should not be taken for granted.

The intense absorption which sets in at about 230 mμ for most of these compounds is believed to be connected with charge-transfer and $d \longrightarrow p$ transitions. It will be the subject of a subsequent communication.

Experimental

Microanalyses (C, H, N) are by Messrs. W. Brown and A. G. Olney of these laboratories.

Platinum Complexes.—These were obtained as described in the references.

Potassium chloroplatinite, K_2PtCl_4. Commercial material was recrystallised from 0·75N-hydrochloric acid, washed with ice-cold water, and dried (Found: Pt, 47·00, 46·99. Calc. for Cl_4K_2Pt: Pt, 47·00%).

Potassium amminotrichloroplatinite,[14] $K[NH_3PtCl_3],H_2O$, was recrystallised from water and air dried (Found: H, 1·4; N, 3·8; Pt, 52·0. Calc. for H_5ONCl_3KPt: H, 1·4; N, 3·7; Pt, 51·9%).

cis-Diamminodichloroplatinum,[15] *cis*-$[(NH_3)_2PtCl_2]$, was thrice recrystallised from water (Found: H, 1·95; N, 9·6; Pt, 65·0.. Calc. for $H_6N_2Cl_2Pt$: H, 2·0; N, 9·3; Pt, 65·0%). The *trans*-isomer [15] was thrice recrystallised from 0·3N-hydrochloric acid (Found: H, 2·0; N, 9·5; Pt, 64·8%).

Triamminochloroplatinum sulphate,[16] $[(NH_3)_3PtCl]_2SO_4,H_2O$. The corresponding chloride prepared by Tschugaev's method had the correct analysis but was faintly yellow (Found: H, 2·8; N, 13·15. Calc. for $H_9N_3Cl_2Pt$: H, 2·9; N, 13·2%). This colour could not be removed by recrystallisation, and was probably caused by contamination with yellow *trans*-$[(NH_3)_2PtCl_2]$, which may be produced during the recrystallisation. The less soluble sulphate was therefore prepared from the sparingly soluble pink $[(NH_3)_3PtCl]_2[PtCl_4]$ by reaction with boiling silver sulphate solution, and obtained as the white monohydrate after recrystallisation from water (Found: H, 2·95; N, 12·65; Pt, 57·3. Calc. for $H_{20}O_5N_6Cl_2SPt_2$: H, 3·0; N, 12·4; Pt, 57·6%).

Tetra-amminoplatinum chloride,[17] $[(NH_3)_4Pt]Cl_2,H_2O$, recrystallised from 3N-ammonia solution in pure white needles which were dried in air (Found: H, 3·5; N, 15·8; Pt, 55·7. Calc. for $H_{14}ON_4Cl_2Pt$: H, 4·0; N, 15·9; Pt, 55·4%).

trans-Bis(di-*n*-pentylamine)dichloroplatinum, *trans*-$[\{(C_5H_{11})_2NH\}_2PtCl_2]$, was kindly supplied by Dr. L. M. Venanzi who prepared it as follows. *trans*-Bis(dimethyl sulphide)dichloroplatinum (2·0 g.) was suspended in di-*n*-butyl ether (*ca.* 50 c.c.) containing di-*n*-pentylamine (2·3 c.c.) and refluxed (2½ hr.). The hot reaction mixture was filtered, and the yellow *product* separated from the filtrate as it cooled. Recrystallised thrice from light petroleum (b. p. 60—80°), it had m. p. 195—197° (Found: C, 41·15; H, 7·7; N, 4·7. $C_{20}H_{46}N_2Cl_2Pt$ requires C, 41·4; H, 8·0; N, 4·8%).

Measurement of Ultraviolet Absorption Spectra.—These were determined on a Unicam S.P. 500 spectrophotometer, modified to take 10 cm. cells. The spectra of two or three different solutions of each substance were determined. When the solutions were stable the extinction coefficients were accurate to about ±1%. All measurements were made at 23° ± 1°.

[13] Pauling, "The Nature of the Chemical Bond," Cornell Univ. Press, Ithaca, 1945.
[14] Cossa, *Ber.*, 1890, **23**, 2503.
[15] "Handbuch der Präparativen Anorganischen Chemie," Ed. Bauer, Enke, Stuttgart, 1953, p. 1181, Method II.
[16] Tschugaev, *J.*, 1915, 1247.
[17] *Inorganic Syntheses*, 1946, **2**, 250.

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The aqueous solutions of K_2PtCl_4 and the ammines, except $[(NH_3)_4Pt]Cl_2$, were not stable and their spectra slowly changed on ageing. These changes were suppressed by hydrochloric acid. They are most probably caused by slow aquations such as those described by Grantham, Elleman, and Martin [18] for the $[PtCl_4]^{2-}$ ion and by K. A. Jensen [19] for the *cis*-diammine, *e.g.*, $[PtCl_4]^{2-} + H_2O \rightleftharpoons [H_2OPtCl_3]^- + Cl^-$. The addition of hydrochloric acid to stabilise the solutions has the danger that chloride ion may add to one or both of the octahedral positions of the platinous complex or replace water molecules already there. This has been observed in solutions containing the $[PdCl_4]^{2-}$ ion,[20] *e.g.*, $[PdCl_4]^{2-} + Cl^- \rightleftharpoons [PdCl_5]^{3-}$. Such reactions should reach equilibrium almost instantaneously. The acid might also abstract ammonia from the ammines, *e.g.*, $[(NH_3)_3PtCl]^+ + HCl \rightleftharpoons [(NH_3)_2PtCl_2] + NH_4^+$, but this reaction should be measurably slow. The fact that 2·0N-hydrochloric acid as solvent gave solutions which were optically stable, or almost so, for the duration of the measurements indicates that neither aquation nor deammination was significant at the the temperatures and concentrations of acid used.

That the addition of chloride ion was also insignificant, if it occurred at all, was shown by observing the wavelengths where the greatest changes in the spectrum of each substance occurred when it was dissolved in pure water. These changes, being reasonably slow, could be accurately extrapolated to zero time. The extrapolated values were in every case identical with those observed in hydrochloric acid solution. General notes on the spectra and stability of the solutions are given below.

Potassium chloroplatinite.[21] Our results are in substantial agreement with those of Babaeva. Solutions of potassium chloroplatinite in 2·0N-hydrochloric acid are stable. Those in weaker acid undergo slow aquation [18] and those in much stronger acid are oxidised to potassium chloroplatinate by air; the rate of oxidation increases with increasing concentration of the acid. The oxidation product was identified by its low solubility and ultraviolet spectrum.

Potassium amminotrichloroplatinite. In neutral solution its spectrum changed for about 19 hr. but in 2·04N-hydrochloric acid the spectrum of a $2{\cdot}76 \times 10^{-3}$M-solution changed only very slowly. The " zero time " spectrum in water and that in 2·04N-hydrochloric acid were in excellent agreement.

cis-*Diamminodichloroplatinum.* In neutral solution the spectrum changed for 7 hr., and it appeared that only one aquated species was formed since there is an isosbestic point at 278 mμ. In 2·0N-hydrochloric acid very little change occurred and in 2·3N-hydrochloric acid the solution was stable. The spectrum in 2·36N-hydrochloric acid was in excellent agreement with the " zero time " spectrum in water.

trans-Diamminodichloroplatinum is so very slightly soluble in water that an accurate spectrum was difficult to obtain, even with 10 cm. cells. It was measured in water by the extrapolation method and in 2N-hydrochloric acid.

Triamminochloroplatinum sulphate. The spectrum of its neutral aqueous solution changed only very slowly as compared with the compounds described above, and so the " zero time " spectrum was obtained accurately without recourse to hydrochloric acid solution.

Tetra-amminoplatinum chloride was stable in neutral aqueous solution and no special precautions were necessary.

trans-*Bis-(di*-n-*pentylamine)dichloroplatinum.* The spectrum was measured in ethanol and in *n*-hexane (" special for spectroscopy ") to observe the effect of solvent on the spectrum.

The Analysis of the Spectra into Gaussian Curves.—The absorption spectra, plotted on a frequency scale, were analysed into a small number of Gaussian error curves, which are known to approximate closely in shape to single absorption bands of transition-metal salts in solution.[22] In this way absorption bands of low intensity, which are concealed by more intense overlapping bands, can be found. The analysis was carried out by trial and error.

The general equation to the Gaussian in terms of extinction coefficient (ε) and frequency (ν) is $\varepsilon = \varepsilon_{max.} \exp[-a(\nu - \nu_0)^2]$, where $\varepsilon_{max.}$, the maximum intensity, occurs at ν_0. Tabulated values of x and z for the equation $z = (2\pi)^{-\frac{1}{2}} \exp(-\frac{1}{2}x^2)$ were taken from mathematical tables,[23]

[18] Grantham, Elleman, and Martin, *J. Amer. Chem. Soc.*, 1955, **77**, 2965.
[19] Jensen, *Z. anorg. Chem.*, 1939, **242**, 87.
[20] Sundaram and Sandell, *J. Amer. Chem. Soc.*, 1955, **77**, 855.
[21] Babaeva, *Doklady Akad. Nauk S.S.S.R.*, 1943, **40**, 61.
[22] Jørgensen, *Acta Chem. Scand.*, 1954, **8**, 1495 and references therein.
[23] Chambers's Six-figure Mathematical Tables, Vol. II, Natural Values, L. J. Comrie, Chambers, Edinburgh and London, 1949, p. 520.

and the most intense peaks were fitted first (*e.g.*, peaks *A* and then *A'*, Figs. 10 and 11). A trial $\varepsilon_{max.}$ was chosen (slightly less than the observed $\varepsilon_{max.}$ if there were neighbouring bands) and the ordinate at $\nu_{max.} = 0$ to plot the Gaussian curve $\varepsilon = \varepsilon_{max.}(2\pi)^{\frac{1}{2}}z = \varepsilon_{max.}\exp(-\frac{1}{2}x^2)$. The scale of the abscissa was chosen to give the best fit to the peak of the experimentally observed

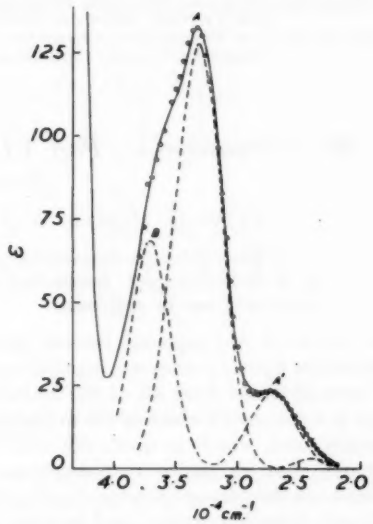

FIG. 10. *Gaussian analysis of the spectrum of* cis-$[(NH_3)_2PtCl_2]$.

——— Experimental. — — — Component Gaussian curves. ○ ○ ○ Sum of Gaussian curves.

spectral band independently of the actual frequency scale, so allowing for the constant (*a*). If a good fit is obtained, the band is evidently single, but if the experimental curve deviates from the Gaussian of best fit, the difference between the Gaussian and experimental curve is plotted

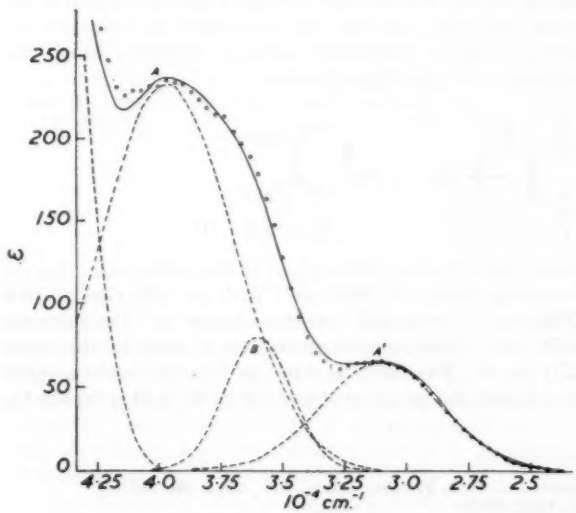

FIG. 11. *Gaussian analysis of the spectrum of* $[(NH_3)_2PtCl]_2SO_4$.

——— Experimental.
— — — Component Gaussian curves.
○ ○ ○ Sum of Gaussian curves.

(*e.g.*, peaks *B*, Figs. 10 and 11) and a Gaussian fitted to the difference curve. Having obtained the best fit to these curves, we can then make a proper allowance for them in fitting the first more intense peaks, and so by repeated approximation the whole absorption curve can be fitted.

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Generally the experimental curves were fitted remarkably closely by the sum of a small number of Gaussian error curves and Fig. 10 and 11 show the best and the worst fittings respectively.

The authors gratefully acknowledge useful discussion with Mr. J. S. Griffith and the experimental assistance of Messrs. D. H. H. Goschenhofer, D. T. Rosevear, and M. L. Searle.

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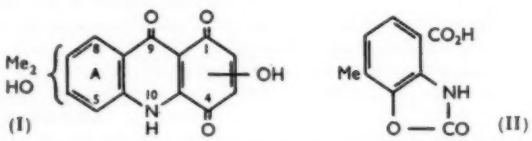
87. *Actinomycin. Part VI.* The Structure and Synthesis of Actinomycinol.*

By W. G. HANGER, W. C. HOWELL, and A. W. JOHNSON.

Actinomycinol, a degradation product of actinomycin, has been shown to be 2 : 5-dihydroxy-3 : 6-dimethylacridone-1 : 4-quinone. The structure has been confirmed by synthesis.

THE action of hot aqueous barium hydroxide on actinomycin produces a crystalline peptide-free hydroxy-quinone, depeptidoactinomycin [1] or actinomycinol.[2] This compound has been obtained from all of the actinomycins examined,[3] suggesting that the chromophore is a common feature in the actinomycin group, although the absorption spectrum of actinomycinol, which is quite different from that of the parent actinomycin, clearly indicates that extensive rearrangement has occurred during the reaction.[2] Actinomycinol is a dihydroxy-quinone, $C_{15}H_{11}O_5N$, containing two *C*-methyl groups. A variety of *N*-and *O*-methyl, acetyl, and benzoyl derivatives of both actinomycinol and dihydroactinomycinol has been prepared by Brockmann and his colleagues.[3,4] The nature of the nucleus of actinomycinol has been the subject of several communications [1,2,5] but the correct partial structure (I), based on acridone-1 : 4-quinone, was suggested by Brockmann and Muxfeldt [6] in 1954. Although actinomycinol did not contain a carboxyl group it was soluble in aqueous sodium hydrogen carbonate, and this was interpreted as indicative of a hydroxyl substituent in the quinone ring (a vinylogous carboxyl system), which was confirmed by formation of a phenazine with *o*-phenylenediamine.

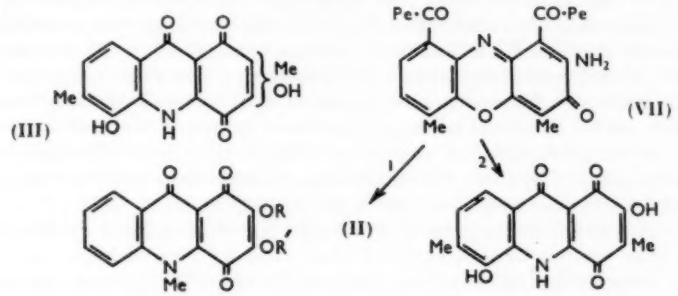


The infrared spectrum of actinomycinol [2] gives some support to the partial structure (I). In the carbonyl region, it shows strong bands at 1664 cm.$^{-1}$ with an inflection at 1656 (quinone-carbonyl groups) and 1616 cm.$^{-1}$ (" extended " amide carbonyl [7]). The spectrum also shows a sharp band at 3278 cm.$^{-1}$ (NH) corresponding to a band in the infrared spectrum of acridone at 3270 cm.$^{-1}$. The band at 810 cm.$^{-1}$ in the actinomycinol spectrum can probably be correlated with the presence of two adjacent $\geqslant$CH groups in the aromatic ring A.

* Part V, *J.*, 1957, 3280.

[1] Brockmann and Grubhofer, *Naturwiss.*, 1950, **37**, 494; *Chem. Ber.*, 1953, **86**, 1407.
[2] Johnson, Todd, and Vining, *J.*, 1952, 2672.
[3] Brockmann and Vohwinkel, *Naturwiss.*, 1954, **41**, 257; *Chem. Ber.*, 1956, **89**, 1373.
[4] Brockmann and Muxfeldt, *Chem. Ber.*, 1956, **89**, 1379.
[5] Brockmann and Budde, *Naturwiss.*, 1953, **40**, 529.
[6] Brockmann and Muxfeldt, *Naturwiss.*, 1954, **41**, 500.
[7] Witkop and Goodwin, *J. Amer. Chem. Soc.*, 1953, **75**, 3371.

In Part IV [8] of this series, we described the degradation of actinomycin B to 7-methylbenzoxazolone-4-carboxylic acid (II). It is evident that the aromatic ring in compound (II) corresponds to ring A of actinomycinol, thus permitting an expansion of the structural formula to (III). The orientation of the remaining hydroxyl and methyl groups was determined by a comparison of the properties of actinomycinol with those of 2-hydroxy-3-methoxy-10-methylacridone-1 : 4-quinone (IV) and the 3-hydroxy-2-methoxy-isomer (V),

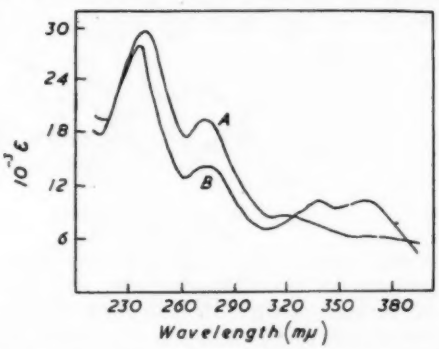


(IV) : R = H, R′ = Me

(V) : R = Me, R′ = H

Reagents: (1) alkaline H_2O_2, then acid hydrolysis; (2) $Ba(OH)_2$.

the structures of which have been proved by Crow and Price [9] in their structural work on melicopicine and related acridone alkaloids. Thus, whereas the quinone (IV) is red, both in the solid state and in solution, the isomer (V) is a greenish-yellow unstable compound giving green solutions in non-polar solvents. The absorption spectrum of the former



Ultraviolet absorption spectra of (1) *actinomycinol and* (2) *3-hydroxy-2-methoxy-10-methylacridone-1 : 4-quinone.*

closely resembles that of actinomycinol (see Figure), and the quinone-carbonyl band in the infrared spectrum is at 1668 cm.$^{-1}$ (actinomycinol, 1664 cm.$^{-1}$) whereas the corresponding band in the spectrum of the isomer (V) is displaced to 1635 cm.$^{-1}$. These observations, which are paralleled by the stabilities of isomers among the safranine dyes,[10] have led us to formulate actinomycinol as 2 : 5-dihydroxy-3 : 6-dimethylacridone-1 : 4-quinone (VI), and the relation between actinomycin [11] (VII) and its degradation products (II) and (VI) is illustrated.

The formation of actinomycinol involves several stages. On the phenoxazin-3-one

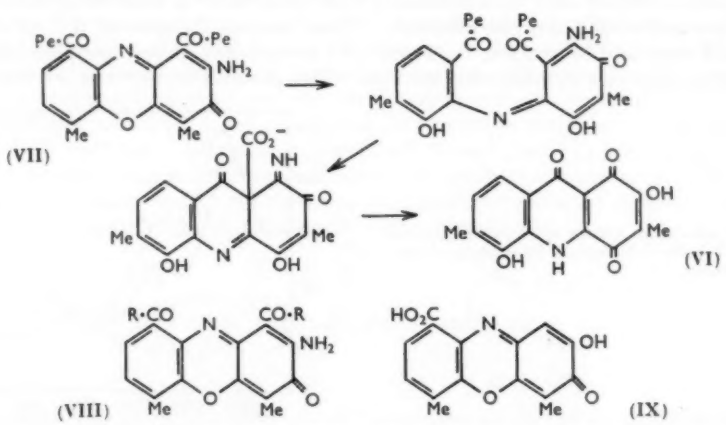
[8] Bullock and Johnson, *J.*, 1957, 1602.
[9] Crow and Price, *Austral. J. Sci. Res.*, 1949, **2**, 282.
[10] Balls, Hewitt, and Newman, *J.*, 1912, **101**, 1840.
[11] Brockmann, Bohnsack, Franck, Gröne, Muxfeldt, and Süling, *Angew. Chem.*, 1956, **68**, 70.

formulation (VII) for actinomycin, the reaction may be regarded as follows, although the precise order of the various stages has not been established and it is not suggested that the postulated intermediates are necessarily capable of separate existence: (1) hydrolysis of the ether (vinylogous ester) bridge of the heterocyclic ring; this is known [12] to occur with alkali under very mild conditions; (2) Dieckmann-type cyclisation, possibly with prior hydrolysis of the amide linkages, in order to relieve the strain in the 2 : 2′-disubstituted quinone anil; [12] (3) decarboxylation after hydrolysis of the peptide chains; (4) hydrolysis of the quinone-amino-group (amide character), and final rearrangement to actinomycinol.

Slight modifications of the actinomycin molecule seriously affect this sequence of events and preclude actinomycinol formation. For example, " deaminoactinomycin " (OH for NH_2 in VII) gives no actinomycinol on treatment with barium hydroxide [13] and likewise we have been unable to obtain actinomycinol from actinocin dimethyl ester [12,13] (VIII; R = OMe) or actinocyldi(glycine methyl ester) [13] (VIII; R = NH·CH_2·CO_2Me), now prepared from methyl 3-hydroxy-4-methyl-2-nitrobenzoate by a modified route.

The reaction of barium hydroxide with actinocin dimethyl ester (VIII; R = OMe) gave 2 : 5-dihydroxy-3-methylbenzoquinone, which also has been isolated by Brockmann and Muxfeldt [14] after reaction of actinomycin C with warm 20% hydrochloric acid. We have isolated this hydroxy-quinone, together with actinocinin [14,15] (IX) from the acid-degradation products of actinocin dimethyl ester.

A preliminary communication [16] of the deduction of structure (VI) was submitted for publication on the same day as one from Brockmann and Muxfeldt [17] who had reached a similar conclusion by careful analysis of the absorption spectrum of dihydroactinomycinol tetramethyl ether on the basis of their " displacement rule." [18]



Structure (VI) for actinomycinol has been confirmed by synthesis. In considering possible approaches, it was decided to build up the acridone system by cyclisation of the appropriate 2-carboxydiphenylamine, which itself could be obtained by condensation of an *o*-chlorobenzoic acid with 2 : 4 : 5-trimethoxy-3-methylaniline. This intermediate, however, proved to be rather inaccessible and in an independent synthesis of actinomycinol [19]

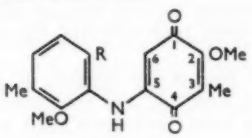
[12] Angyal, Bullock, Hanger, Howell, and Johnson, *J.*, 1957, 1592.
[13] Brockmann and Muxfeldt, *Angew. Chem.*, 1956, **68**, 69.
[14] *Idem, ibid.*, p. 67.
[15] Brockmann and Gröne, *ibid.*, p. 66.
[16] Angyal, Bullock, Hanger, and Johnson, *Chem. and Ind.*, 1955, 1295.
[17] Brockmann and Muxfeldt, *Angew. Chem.*, 1955, **67**, 617.
[18] Brockmann, Muxfeldt, and Haese, *Chem. Ber.*, 1956, **89**, 2174.
[19] Brockmann and Muxfeldt, *Angew. Chem.*, 1955, **67**, 618; *Chem. Ber.*, 1956, **89**, 1397.

the German workers substituted 4 : 5-dimethoxy-3-methyl-2-nitroaniline as the second component.

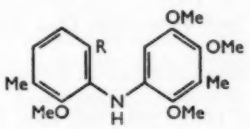
The difficulty of preparing these intermediates led us to investigate the formation of the arylaminoquinones by addition of suitably substituted anilines to *p*-benzoquinones. In the first instance it was proposed to introduce the carboxyl group (R = CO_2H in X) required for acridone formation by a separate process after the addition, but later the anthranilic acid was added directly to the quinone. These methods have the advantage that the requisite quinone, 2-methoxy-3-methyl-*p*-benzoquinone,[20] was obtainable from the intermediate amine, 2-methoxy-*m*-toluidine, by oxidation with chromic acid, an observation which suggested that actinomycin might be formed biogenetically by dimerisation of a benzenoid intermediate, as proved to be the case. Although the normal addition of arylamines to simple quinones affords both mono- and di-adducts,[21] only monoaddition occurs with 2-methoxy-3-methyl-*p*-benzoquinone, and the initial aminoquinol is oxidised immediately by the original quinone to give the adduct (X; R = H). Demethylation and/or demethoxylation has been reported in certain cases during the addition of amines to quinones under forcing conditions [22] but no such reaction was observed in the present instance.

In predicting the point of addition of the amine to 2-methoxy-3-methyl-*p*-benzoquinone it was expected that the effect of the methoxyl group was to neutralise partly the electron-withdrawing properties of the quinonoid 4-carbonyl group (vinylogous ester system) and the overriding directional influence for nucleophilic addition was therefore exerted by the 1-carbonyl group, causing the amine to add at $C_{(5)}$ as shown in (X; R = H). This was verified by hydrolysis of the adduct with sulphuric acid, 2 : 5-dihydroxy-3-methylbenzoquinone being obtained (dimethyl ether,[23] m. p. 104—105°).

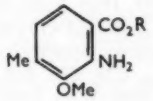
The quinone (X; R = H) was methylated reductively before attempts were made to introduce the carbonyl bridge, and the product, 2 : 4 : 5 : 2′-tetramethoxy-3 : 3′-dimethyldiphenylamine (XI; R = H) was treated with oxalyl chloride in the presence of aluminium chloride,[24] but yielded a complex mixture from which we were unable to isolate any of the desired products. In another attempt carbonyl chloride was substituted for oxalyl chloride but to no avail.



(X)



(XI)



(XII)

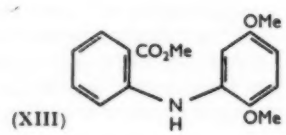
The synthesis was therefore modified in such a way that the potential carbonyl group of the acridonequinone was included in the original amine before addition to the quinone, *i.e.*, the substituted anthranilic acid or its ester (XII; R = H or Me) was used in the addition reaction. The addition of anthranilic acids to benzoquinones is a well-known reaction, and mono- and di-adducts can be formed. In a recent study,[25] Acheson and Sansom reported only the diaddition product from anthranilic acid and *p*-benzoquinone but we have found that the monoaddition product [26] is obtainable if addition is carried out in aqueous acetic acid at room temperature and that it can be reductively methylated to 2 : 5-dimethoxy-2′-methoxycarbonyldiphenylamine (XIII).

The 3-methoxy-4-methylanthranilic acid (XII; R = H) required for the synthesis of

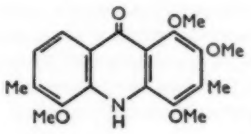
[20] Majima and Okazaki, *Ber.*, 1916, **49**, 1482.
[21] Suida and Suida, *Annalen*, 1918, **416**, 113.
[22] Anslow and Raistrick, *J.*, 1939, 1446.
[23] Anslow, Ashley, and Raistrick, *J.*, 1938, 439.
[24] Stollé, *Ber.*, 1913, **46**, 3915; *J. prakt. Chem.*, 1922, **105**, 137.
[25] Acheson and Sansom, *J.*, 1955, 4440.
[26] Astre, *Bull. Soc. chim. France*, 1896, **15**, 1025.

XUM

actinomycinol was obtained from 7-methoxy-6-methylisatin,[8] itself prepared from 2-methoxy-*m*-toluidine, by oxidation with alkaline hydrogen peroxide according to the method of Baker *et al.*[27] Although the addition of unsubstituted anthranilic acid or its methyl ester to *p*-benzoquinone is complete after one hour at room temperature, addition of the acid or ester (XII; R = H or Me) to 2-methoxy-3-methylbenzoquinone was much slower and even at 60° in aqueous ethanol required several days. The product (X; R = CO_2H) was reductively methylated to yield the ester (XI; R = CO_2Me) which was hydrolysed to the acid (XI; R = CO_2H). This acid was cyclised by phosphorus oxychloride, and the 9-chloroacridine derivative (not isolated) was hydrolysed with dilute acid to a product, m. p. 158—159°, presumably (XIV), dihydroactinomycinol tetramethyl ether, or an isomer.



(XIII)



(XIV)

Reductive methylation[4] of actinomycinol (from actinomycin) gives a compound, m. p. 183—184°, also claimed to be dihydroactinomycinol tetramethyl ether, but the structural difference between this and the synthetic product is still under investigation. The synthetic acridone of m. p. 158—159° was demethylated completely by hydrobromic acid or pyridine hydrobromide and, after aerial oxidation of a weakly alkaline solution of the product, the actinomycinol so obtained was identical with that[2] derived from actinomycin in infrared, ultraviolet, and visible absorption spectra.

Experimental

95% Ethanol was used as solvent in determinations of absorption spectra, and Nujol mulls were used for infrared spectra, except where otherwise stated.

Actinomycinol B.—Prepared from actinomycin B as described in Part II,[2] it formed red needles after sublimation at 160°/10^{-4} mm. (Found: C, 63·0; H, 4·0; N, 5·0. Calc. for $C_{15}H_{11}O_5N$: C, 63·2; H, 3·9; N, 4·9%). The infrared spectrum showed max. at 3279, 2660, 2330, 1664, 1616, 1548, 1357, 1285, 1259, 1220, 1174, 1109, 1049, 1015, 980, 943, 915, 837, 812, 773, 750, 714, and 670 cm.$^{-1}$.

2-Hydroxy-3-methoxy-10-methylacridone-1 : 4-quinone[9] formed red needles, m. p. 236—238°, $\lambda_{max.}$ 235, 276, 336, and 365—368 mμ (log ε 4·44, 4·14, 4·00, and 4·01 respectively), $\nu_{max.}$ at 1668, 1600, 1580, 1520, 1410, 1310, 1280, 1260, 1205, 1165, 1135, 1095, 1060, 1040, 1020, 955, 930, 865, 820, 790, 770, 755, and 745 cm.$^{-1}$.

3-Hydroxy-2-methoxy-10-methylacridone-1 : 4-quinone[9] had infrared max. at 3250, 1635, 1575, 1540, 1475, 1300, 1255, 1220, 1190, 1165, 1130, 1100, 1040, 980, 945, 920, 860, 805, 780, 770, 765, 725, and 708 cm.$^{-1}$.

3-Benzyloxy-4-methyl-2-nitrobenzoic Acid.—A solution of potassium hydroxide (1·8 g.) in methanol (20 c.c.) was added to methyl 3-hydroxy-4-methyl-2-nitrobenzoate[12] (5·67 g.) and benzyl chloride (3·8 g.) in methanol (15 c.c.), and the mixture heated under reflux for 19 hr. The cooled mixture was diluted with water (200 c.c.) and extracted with ether (3 × 100 c.c.) and the combined ethereal extracts were washed and dried. Acidification of the aqueous layer and washings gave the unchanged hydroxy-ester (1·02 g.). After removal of the solvent from the ethereal solution, the oily residue so obtained was hydrolysed directly by boiling 20% aqueous sodium hydroxide (50 c.c.) for 5 min. After cooling, the product was diluted with water (150 c.c.) and then extracted with ether to remove neutral products. Acidification of the aqueous layer gave an almost quantitative (6·30 g.) yield, allowing for unchanged starting material, of the *product* which crystallised from methanol in colourless prisms, m. p. 176—177° (Found, on a sample sublimed at 160°/0·05 mm.: C, 62·7, H, 4·35; N, 5·1. $C_{15}H_{13}O_5N$ requires C, 62·7; H, 4·55; N, 4·9%).

N-[3-Benzyloxy-4-methyl-2-nitrobenzoyl]glycine Methyl Ester.—The foregoing acid (6·32 g.) was

[27] Baker, Schaub, Joseph, McEvoy, and Williams, *J. Org. Chem.*, 1952, **17**, 141.

suspended in benzene and heated under gentle reflux with thionyl chloride (21 g.) for 1 hr. The resulting solution was concentrated under reduced pressure to remove the excess of thionyl chloride, and the residual acid chloride, which solidified on cooling, was redissolved in dry benzene (50 c.c.). Finely powdered glycine methyl ester hydrochloride (2·8 g.) was added and the mixture heated under reflux for 20 hr., then any undissolved material was separated from the hot solution. The filtrate was cooled and the crystals which separated were removed and washed with benzene and ether. By gradual concentration of the mother-liquors a further quantity of the product was obtained and the combined product (5·55 g., 70%) was recrystallised from aqueous ethanol, to give the *ester* as colourless feathery needles, m. p. 123—123·5° (Found: C, 60·5; H, 5·2; N, 7·9. $C_{18}H_{18}O_6N_2$ requires C, 60·3; H, 5·1; N, 7·8%).

N-(3-*Hydroxy*-4-*methylanthraniloyl*)*glycine Methyl Ester Hydrochloride*.—The nitro-ester (2·47 g.) from the preceding experiment was suspended in ethanol (25 c.c.) and hydrogenated over Raney nickel (1 g.) at atmospheric pressure and room temperature. After the absorption of hydrogen had ceased, the catalyst was separated and the filtrate diluted with ether (100 c.c.) and saturated with dry hydrogen chloride. The *amine hydrochloride* (1·58 g., 83%) slowly separated after gradual dilution of the solution with ether. Recrystallised from ethanol–ether it had m. p. 174—174·5° (decomp.) (Found: C, 47·9; H, 5·5; Cl, 12·85. $C_{11}H_{15}O_4N_2Cl$ requires C, 48·1; H, 5·5; Cl, 12·9%).

Actinocyldi(*glycine Methyl Ester*).—*N*-(3-Hydroxy-4-methylanthraniloyl)glycine methyl ester (0·438 g.) was dissolved in phosphate buffer (500 c.c.; pH 7·1) and kept at 40° while a solution of potassium ferricyanide (1·05 g.) in water (40 c.c.) was added, dropwise with stirring. After cooling, the product which had separated as a bright orange flocculent solid was collected, washed, and dried. It crystallised from chloroform (hot extraction from a Soxhlet thimble), to give *actinocyldi*(*glycine methyl ester*) (0·29 g., 78%) as fine orange needles, decomp. at 283—285° (Found: C, 56·5; H, 4·9; N, 11·8. $C_{22}H_{22}O_8N_4$ requires C, 56·2; H, 4·7; N, 11·9%), $\lambda_{max.}$ in MeOH, 237, 423, and 443 mμ (log ε 4·61, 4·45, and 4·48 respectively), in dioxan 239, 425, and 445 mμ (log ε 4·59, 4·44, and 4·46 respectively).

Action of Barium Hydroxide on Actinocin Dimethyl Ester.—A suspension of actinocin dimethyl ester [12, 13] (107 mg.) in 2N-barium hydroxide (20 c.c.) was heated under reflux for 4·5 hr. The ester slowly dissolved and purple-brown solid was precipitated. This was separated, washed with water, and dissolved in 2N-hydrochloric acid (30 c.c.) to give a brownish-orange solution, which was extracted with chloroform (3 × 50 c.c.). Removal of the solvent from the washed and dried extract gave a brown solid (19·5 mg.) which, unlike actinomycinol, was completely soluble in cold ethyl acetate. This material crystallised from nitrobenzene in copper-bronze plates which were further purified by sublimation at 90°/0·05 mm. The orange-red prisms of 2 : 5-dihydroxy-3-methylbenzoquinone thus obtained had m. p. 175—177° (partial decomp.) and formed a violet solution in dilute alkali (Found: C, 54·8; H, 4·1. Calc. for $C_7H_6O_4$: C, 54·55; H, 3·9%), $\lambda_{max.}$ 288 and 416 mμ (log ε 4·35 and 2·46), in chloroform 289 and 423 mμ (log ε 4·36 and 2·43).

Action of Hydrochloric Acid on Actinocin Dimethyl Ester.—The ester (313 mg.) was heated in 20% hydrochloric acid (60 c.c.) under reflux for 1 hr. On cooling, the deep red solution deposited very dark green crystals (232 mg.) which were separated, washed, and dried. The filtrate and washings were extracted with chloroform (4 × 100 c.c.), and the combined chloroform extracts washed, dried, and evaporated, to yield a crimson solid (20 mg.). This was sublimed and gave 2 : 5-dihydroxy-3-methyl-*p*-benzoquinone (8 mg.) as brownish-orange crystals, m. p. 174—177° (decomp.). The dark precipitate obtained as above was dissolved in saturated sodium hydrogen carbonate solution (50 c.c.) and then extracted with chloroform and ether. The aqueous solution was made slightly acid by addition of dilute hydrochloric acid, a dark red solid separating. It was extracted into chloroform (3 × 75 c.c.) and, by gradual concentration of the washed and dried chloroform solution, several crops of crimson needles of *actinocinin* [14, 15] were obtained which decomposed at 260° (Found, in a sample dried at 70° *in vacuo*: C, 62·9; H, 3·9; N, 5·0. $C_{15}H_{11}O_5N$ requires C, 63·2; H, 3·9; N, 4·9%). Light absorption max. were at 236 and 415 mμ (log ε 4·39 and 4·25).

2-*Methoxy*-3-*methyl*-p-*benzoquinone*.—A solution of 2-methoxy-*m*-toluidine (40 g.) in 10N-sulphuric acid (1 l.) was cooled to 0° and stirred vigorously while a solution of sodium dichromate (40 g.) in water (225 c.c.) was added during 1 hr. After an additional 5 hours' stirring the mixture was kept at <10° for 12 hr. It was then treated with a second portion of sodium dichromate (80 g.) in water (400 c.c.), as before. Stirring was discontinued after 3 hr. and the

black viscous mixture was extracted with ether (5 × 400 c.c.). The ethereal extract was washed and dried and the solvent distilled off through a small Vigreux column. Distillation of the residue under reduced pressure gave 2-methoxy-3-methyl-*p*-benzoquinone (14·7 g., 33%) as an orange-yellow oil, b. p. 104—105°/12 mm., which rapidly solidified to a yellow crystalline mass, m. p. 19—20° (Found: C, 63·4; H, 5·4. Calc. for $C_8H_8O_3$: C, 63·2; H, 5·3%).

2-*Methoxy*-5-(2-*methoxy*-m-*toluidino*)-3-*methyl*-p-*benzoquinone*.—To a suspension of 2-methoxy-3-methyl-*p*-benzoquinone (2·2 g.) in water (220 c.c.) was added a solution of 2-methoxy-*m*-toluidine (1 g.) in acetic acid (0·5 c.c.) and water (5 c.c.). Darkening was observed immediately and, within a short time, a purple precipitate had been formed. After the mixture had been shaken at room temperature for 5 hr. the precipitate was separated, washed with water, and dried (1·87 g.). In view of the ready polymerisation of the product it was used without further purification in the next stage (below). It had absorption max. at 520, 327, and 257 mμ (log ε 3·49, 3·88, and 4·14 respectively) and inflections at 333 and 276 mμ (log ε 3·87 and 4·03).

2 : 4 : 5 : 2′-*Tetramethoxy*-3 : 3′-*dimethyldiphenylamine*.—An ethanolic solution (75 c.c.) of the foregoing anilino-quinone (1 g.) was hydrogenated in the presence of Adams platinum catalyst (0·15 g.) for 2 hr., during which the colour changed from intense purple to pale green. Dimethyl sulphate (2 c.c.) and a suspension of finely ground anhydrous potassium carbonate (5 g.) and further catalyst (0·1 g.) in ethanol (50 c.c.) were then added to the hydrogenation product while still in an atmosphere of hydrogen. Hydrogenation was continued for a further 24 hr. After filtration through " Supercel " the ethanolic solution was almost colourless. As inorganic material was present after removal of the solvent, the dried residue was extracted with chloroform (4 × 50 c.c.), and the solvent removed from the combined extracts, to give a pale yellow oil (1·1 g.) which slowly solidified. Repeated recrystallisation from methanol gave colourless prisms of the *diphenylamine*, m. p. 107° (Found: C, 68·4; H, 7·4; N, 4·5. $C_{18}H_{23}O_4N$ requires C, 68·1; H, 7·3; N, 4·4%), $\lambda_{max.}$ 302 and 277 mμ (log ε 3·87 and 4·10), $\nu_{max.}$ 3440, 1605(s), 1587, 1510, 1488, 1455, 1420, 1385, 1370, 1360, 1310(s), 1250, 1225(s), 1205(s), 1162(s), 1130, 1090(s), 1060(s), 1005(s), 994(s), 852, 830, 808, 783(s), 750, and 712 cm.$^{-1}$.

2 : 5-*Dihydroxy*-3-*methyl*-p-*benzoquinone*.—2-Methoxy-5-(2-methoxy-*m*-toluidino)-3-methyl-*p*-benzoquinone (0·34 g.) was heated under reflux with 10N-sulphuric acid (7 c.c.) for 4 min. Initially the amino-quinone floated on the sulphuric acid as a purple oil but after 2—3 min. it dissolved and an orange sublimate collected in the condenser. The mixture was extracted with chloroform (5 × 25 c.c.), and the extracts were washed and evaporated *in vacuo*. Sublimation (95°/2 mm.) of the brown residue gave 2 : 5-*dihydroxy*-3-*methyl*-p-*benzoquinone* as orange prisms (0·1 g.), m. p. and mixed m. p. 173—175° (with sublimation) (Found: C, 54·7; H, 3·9. $C_7H_6O_4$ requires C, 54·6; H, 3·9%). This quinone gave a deep red ferric reaction and a violet colour with dilute alkali.

2 : 5-*Dimethoxy*-3-*methyl*-p-*benzoquinone*.—2 : 5-Dihydroxy-3-methyl-*p*-benzoquinone (34 mg.) in ethanol (15 c.c.) was shaken with dimethyl sulphate (0·2 c.c.) and anhydrous potassium carbonate (0·5 g.) at room temperature for 3 days. The solid was separated, the filtrate evaporated to dryness, and the residue treated with dilute hydrochloric acid (2 c.c.) and extracted with chloroform (3 × 10 c.c.). From the extract a yellow residue (3 mg.) was obtained. After two sublimations (95°/2 mm.), 2 : 5-dimethoxy-3-methyl-*p*-benzoquinone was obtained as golden-yellow needles (2 mg.), m. p. 104—105°. The brown solid separated as above was acidified and extracted with chloroform. After working up as described above, unchanged 2 : 5-dihydroxy-3-methylbenzoquinone was obtained as orange prisms (18 mg.), m. p. and mixed m. p. 173—174°.

2-2′-*Carboxyanilino*-1 : 4-*benzoquinone*.—To a suspension of *p*-benzoquinone (2·36 g.) in water (240 c.c.) was added anthranilic acid (1·0 g.) in acetic acid (2 c.c.). On addition of the acid an immediate purple colour developed and a brown solid separated. The reaction was complete after 4 hours' shaking at room temperature. Then the dark brown solid (1·8 g.) was separated and dried (P_2O_5) and used without further purification.

2 : 5-*Dimethoxy*-2′-*methoxycarbonyldiphenylamine*.—The foregoing quinone addition compound (1·8 g.) was dissolved in ethanol and hydrogenated in the presence of Adams platinum catalyst (0·2 g.). When hydrogenation was complete, dimethyl sulphate (4 c.c.) and a suspension of finely powdered anhydrous potassium carbonate (9 g.) and platinum catalyst (0·2 g.) in ethanol (90 c.c.) were added, the atmosphere of hydrogen being maintained. Hydrogenation was then continued for a further 60 hr. On exposure to air the resulting solution remained colourless and the residue obtained from filtration was washed with ethanol and then water, and the combined filtrates were evaporated *in vacuo* until no alcohol remained and oily green

drops appeared in the aqueous solution. Extraction with chloroform (5 × 25 c.c.) gave, after removal of the solvent and sublimation at 170°/1 mm., a pale green oil (2·2 g.) which slowly crystallised. Several recrystallisations from methanol gave the *diphenylamine ester* (1·7 g.) as colourless plates m. p. 65—67° (Found: C, 66·3; H, 5·7; N, 4·8. $C_{16}H_{17}O_4N$ requires C, 66·9; H, 5·95; N, 4·9%), $\nu_{max.}$ 1683(s), 1600(s), 1577(s), 1522(s), 1492, 1330, 1310, 1282, 1259(s), 1230, 1215, 1198, 1162, 1128, 1083, 1055, 1043, 1020, 961, 951, 914, 892, 852(s), 824, 803(s), 755, and 723 cm.$^{-1}$. A determination in hexachlorobutadiene revealed additional bands at 3300, 2941, 2845, 1451, 1432, and 1418 cm.$^{-1}$.

3-*Methoxy*-4-*methylanthranilic Acid*.—To a stirred aqueous solution of 7-methoxy-6-methylisatin [8] (8 g.) in 5% aqueous sodium hydroxide (75 c.c.) was added, during 20 min., a 30% solution of hydrogen peroxide (17 c.c.), the temperature rising to a maximum of 51° and the colour diminishing from the initial orange to pale yellow. After a further 20 min. the solution was acidified to pH 4 with dilute hydrochloric acid. The pale fawn solid which had been precipitated was separated, washed with a little water (10 c.c.), and dried. Crystallisation from toluene (after removal of insoluble material) afforded the acid as brown needles (5·4 g., 70%). Sublimation at 120°/1 mm. gave the pure *acid* as pale yellow needles, m. p. 162° (Found: C, 59·7; H, 6·0; N, 7·8. $C_9H_{11}O_3N$ requires C, 59·7; H, 6·1; N, 7·7%), $\nu_{max.}$ 3420, 3330, 2560, 2490, 1650(s), 1612, 1588(s), 1540, 1450(s), 1410, 1300(s), 1250, 1235(s), 1216, 1167, 1130, 1060, 1010(s), 933, 868, 825, 728(s), 718(s), and 705 cm.$^{-1}$.

To a solution of the acid (0·1 g.) in ether (25 c.c.) was added excess of ethereal diazomethane, and the mixture kept at room temperature for 1 hr. Removal of the solvent gave a white solid (0·11 g.) which on sublimation at 80°/1 mm. gave *methyl* 3-*methoxy*-4-*methylanthranilate* (0·1 g.) as white prisms, m. p. 88—89° (Found: C, 61·7; H, 6·8; N, 7·2. $C_{10}H_{13}O_3N$ requires C, 61·5; H, 6·7; N, 7·2%), $\nu_{max.}$ (i) 3465, 3360, 1690(s), 1620(s), 1600, 1550, 1305, 1235, 1180(s) 1165, 1090, 1060(s), 995, 975, 945, 860, 795, 772(s), 752(s), and 720 cm.$^{-1}$, (ii) in hexachlorobutadiene, additionally at 2936, 2860, 1450, and 1430 cm.$^{-1}$.

2-*Carboxy*-2′ : 4′ : 5′ : 6-*tetramethoxy*-3′ : 5-*dimethyldiphenylamine*.—A solution of 4-methyl-3-methoxyanthranilic acid (0·60 g.) and 2-methoxy-3-methyl-*p*-benzoquinone (1·1 g.) in methanol (25 c.c.) was heated under reflux for 4 days. After being kept at room temperature for 1 day, the deep red solution was concentrated to 10 c.c. and taken up in benzene (100 c.c.). After several washings with water the cherry-red extract was cautiously evaporated to dryness *in vacuo*, to give a dark red viscous oil. This material was hydrogenated in absolute ethanol (90 c.c.) at room temperature and pressure over Adams platinum catalyst (0·15 g.). After 30 min., anhydrous potassium carbonate (9 g.), dimethyl sulphate (4 c.c.), and additional catalyst (0·15 g.) were quickly added and hydrogenation continued for 3 days. Additional portions of potassium carbonate (9 g.), dimethyl sulphate (4 c.c.), and catalyst (0·1 g.) were added and hydrogenation continued for 24 hr. The catalyst and other insoluble material were removed and the ethanol was evaporated from the filtrate. The aqueous residue was extracted with chloroform (5 × 20 c.c.). Evaporation of the solvent from the combined extracts gave a red oil. Acidification and chloroform-extraction of the aqueous layer gave *ca.* 40 mg. of red acidic material. The above red oil in chloroform (25 c.c.) was extracted with concentrated hydrochloric acid (4 × 15 c.c.). The combined acid extracts were diluted with water (100 c.c.), and the aqueous solution re-extracted with chloroform (5 × 15 c.c.). After removal of the chloroform, brown crystals (0·15 g.) were obtained which recrystallised from methanol to give colourless plates of methyl 3-methoxy-4-methylanthranilate, m. p. and mixed m. p. 88—89°. The chloroform solution, after extraction with concentrated acid, was washed with water and evaporated, whereupon the crude diphenylamine ester was obtained as a dark oil. This oil was heated under reflux with ethanol (25 c.c.) and 2N-sodium hydroxide (15 c.c.) for 8 hr., the ethanol evaporated, and non-acidic material removed in chloroform. The alkaline solution was diluted with 2N-hydrochloric acid (15 c.c.) and extracted with chloroform. Removal of the chloroform *in vacuo* gave a brown acidic oil which was subjected to a counter-current distribution (48 transfers) using the solvent system, ethyl acetate–phosphate buffer solution (pH 6·9; M/15-solution). To each of the resultant fractions, 3N-sulphuric acid (2 c.c.) was added and, after being shaken, the organic layers were separated, washed, and evaporated. Tubes 37—47 contained crystalline residues which were combined (0·61 g.) and crystallised from ether–methanol to furnish the *carboxydiphenylamine* as colourless prisms, m. p. 168—169° (decomp.) (Found: C, 63·3; H, 6·1; N, 4·1. $C_{19}H_{23}O_6N$ requires C, 63·15; H, 6·4; N, 3·9%), main infrared bands at 3200, 1675, 1605, 1568, 1498, 1218, 1192, and 848 cm.$^{-1}$.

XUM

1 : 2 : 4 : 5-*Tetramethoxy*-3 : 6-*dimethylacridone*.—The above acid (68 mg.) was heated under reflux with phosphorus oxychloride (0·5 c.c.) for 1 hr. The deep red solution so obtained was evaporated to dryness *in vacuo* and gave a red residue, to which 0·5N-hydrochloric acid (5 c.c.) was added and the mixture was heated to 100° for 30 min. Chloroform extraction (5 × 10 c.c.) of the cooled solution gave an orange-red extract which was washed with sodium carbonate (2 × 10 c.c.) and then water (3 × 5 c.c.), and the solution (yellow, with green fluorescence) was evaporated to dryness, an orange solid (60 mg.) being obtained. Although this product crystallised from ether the product still contained a small amount of a red impurity. Chromatography on magnesium trisilicate with benzene–ethanol (98 : 2) as solvent gave a yellow eluate (150 c.c.) having a pronounced fluorescence, and evaporation of the solvent furnished a yellow crystalline *acridone* (55 mg.), m. p. 158—159° after crystallisation from methanol–light petroleum (b. p. 60—80°) (Found: C, 67·0; H, 6·3; N, 4·4; MeO, 36·5. $C_{19}H_{21}O_5N$ requires C, 66·5; H, 6·2; N, 4·1; 4MeO, 36·1%), $\nu_{max.}$ 263, 314, and 390 mμ (log ε 4·78, 3·46, and 3·85 respectively).

2 : 5-*Dihydroxy*-3 : 6-*dimethylacridone*-1 : 4-*quinone* (*Actinomycinol*).—The above tetramethoxyacridone (75 mg.) was heated under reflux with concentrated hydrobromic acid (2 c.c.) for 1 hr. After cooling, the mixture was poured into 0·1N-sodium hydroxide (100 c.c.). A brownish suspension was formed and the solution was rendered alkaline by adding 1N-aqueous sodium hydroxide (20 c.c.), whereupon the solid dissolved to give a port-wine-coloured solution which was aerated vigorously for 1 hr. The resulting solution was made weakly acid and exhaustively extracted with chloroform. The combined extracts were dried (Na_2SO_4) and evaporated to dryness to give a dark solid (29 mg.). Crystallisation from 50% aqueous acetic acid (20 c.c.) gave *actinomycinol* as red needles (17 mg.) which were purified further by sublimation at 160°/10^{-4} mm. (Found: C, 62·9; H, 4·0; N, 4·6. $C_{15}H_{11}O_5N$ requires C, 63·15; H, 3·9; N, 4·9%), $\lambda_{max.}$ 245, 276, 322, 370, and 476 mμ (log ε 4·47, 4·28, 3·86, 3·72, and 3·59 respectively). The infrared spectrum of the synthetic specimen showed max. at 3280, 2660, 2330, 1660, 1614, 1545, 1355, 1290, 1255, 1175, 1110, 1047, 1015, 982, 944, 912, 810, 770, 750, and 715 cm.$^{-1}$. Actinomycinol from actinomycin showed ultraviolet max. at 244, 277, 322, 370, and 475 mμ (log ε 4·49, 4·28, 3·91, 3·75, and 3·60), and infrared max. at 3279, 2660, 2330, 1664, 1616, 1548, 1357, 1285, 1259, 1174, 1110, 1049, 1015, 980, 943, 915, 812, 773, 750, and 714 cm.$^{-1}$.

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88. *Synthesis of Some* 1 : 2- *and* 7 : 8-*Benzophenanthridines.*

By K. W. Gopinath, T. R. Govindachari, K. Nagarajan, and K. K. Purushothaman.

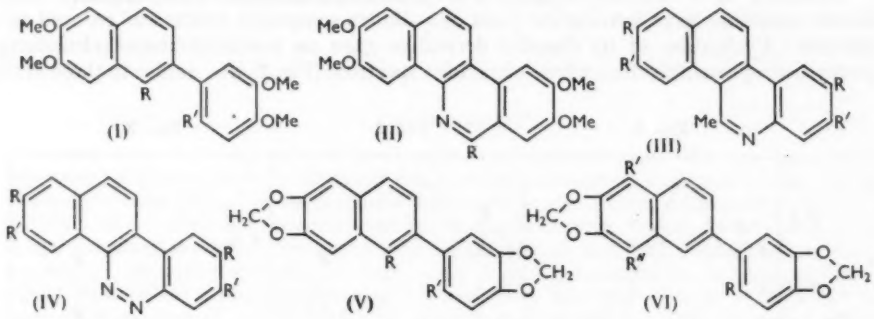
6-(3 : 4-Dimethoxyphenyl)-2 : 3-dimethoxynaphthalene yields a mixture of the 5- and the 6′-mononitro-compound (I) and (Ib), reduced to the corresponding amines. The formyl and acetyl derivatives of the amines are cyclised to tetramethoxybenzophenanthridines. Diazotisation of the amine (Ic) yields the 5 : 6-diazachrysene (IVa). Nitration of 2 : 3-methylenedioxy-6-(3 : 4-methylenedioxyphenyl)naphthalene leads to the 6′-nitro-derivative (V), which through the acetyl derivative of the amine gives the 7 : 8-benzophenanthridine (IIIa). Diazotisation of the amine (Va) yields a diazachrysene (IVb). The dinitration product of the methylenedioxynaphthalene is assigned a probable structure.

In connexion with work on some 1 : 2-benzophenanthridine alkaloids, we had occasion to study the nitration of 6-(3 : 4-dimethoxyphenyl-2 : 3-dimethoxy)- and 2 : 3-methylenedioxy-6-(3 : 4-methylenedioxyphenyl)-naphthalene which were readily available.[1] We

[1] Gopinath, Govindachari, Nagarajan, and Purushothaman, *J.*, 1957, 1144.

present below an account of the products and the benzophenanthridines obtained from them.

6-(3 : 4-Dimethoxyphenyl)-2 : 3-dimethoxynaphthalene gave two mononitro-derivatives. One is 2-(3 : 4-dimethoxyphenyl)-6 : 7-dimethoxy-1-nitronaphthalene (I), since cyclisation of the formyl derivative of the derived amine (Ia) yielded the known 2′ : 3′ : 6 : 7-tetramethoxy-1 : 2-benzophenanthridine [2] (II). Catalytic reduction of these nitro-compounds proceeded best in benzene solution, use of alcohol or acetic acid as solvent



	R	R′
(I)	NO_2	H
(Ia)	NH_2	H
(Ib)	H	NO_2
(Ic)	H	NH_2
(II)	H	—
(IIa)	Me	—

	R	R′
(III)	OMe	OMe
(IIIa)	$-CH_2O_2-$	
(IV)	H	H
(IVa)	OMe	OMe
(IVb)	$-CH_2O_2-$	

	R	R′ (or R″)
(V)	H	NO_2
(Va)	H	NH_2
(Vb)	NO_2	H
(VI)	NO_2	NO_2
(VIa)	NH_2	NH_2

giving very poor yields. The acetyl derivative of the base (Ia) likewise furnished the 9-methylbenzophenanthridine (IIa). The other product of mononitration is evidently 6-(4 : 5-dimethoxy-2-nitrophenyl)-2 : 3-dimethoxynaphthalene (Ib), since reduction to the amine (Ic), acetylation, and cyclisation yielded 2 : 3 : 2′ : 3′-tetramethoxy-9-methyl-7 : 8-benzophenanthridine (III). The corresponding formamide did not undergo cyclisation, because of insufficient activation at the 1-position of the naphthalene. 2-Acetamidodiphenyl is known to give 9-methylphenanthridine readily whereas the 2-formyl derivative is difficult to cyclise.[3]

An attempted Sandmeyer reaction on 6-(6-amino-3 : 4-dimethoxyphenyl)-2 : 3-dimethoxynaphthalene (Ic) resulted in a compound, $C_{20}H_{18}O_4N_2$, whose ultraviolet spectrum (Fig. 1) showed the presence of an extended chromophore. The compound is assigned the structure, 2 : 3 : 8 : 9-tetramethoxy-5 : 6-diazachrysene (IVa), in analogy with the formation of cinnolines by diazotisation of 2-aminostyrenes.[4] The parent diazachrysene (IV) is unknown.[5]

Nitration of 2 : 3-methylenedioxy-6-(3 : 4-methylenedioxyphenyl)naphthalene has been reported [6] to yield the nitro-derivative (V), m. p. 225—228°. Repetition of the nitration and repeated recrystallisation of the product from acetic acid gave a purer specimen, of m. p. 241—242° which could not be improved further. Reduction to the amine (Va) and cyclisation of the acetyl derivative yielded 9-methyl-2 : 3-2′ : 3′-bismethylenedioxy-7 : 8-benzophenanthridine (IIIa) having an ultraviolet spectrum (Fig. 2) very similar to that of the tetramethoxy-analogue (III). The formyl derivative of the amine (Va), as expected,

[2] Bailey, Robinson, and Staunton, *J.*, 1950, 2277.
[3] Whaley and Govindachari, "Organic Reactions," John Wiley & Sons, Inc., New York, 1951, Vol. VI, p. 131.
[4] Simpson, *J.*, 1943, 447.
[5] Allen, "Six Membered Nitrogen Compounds with Four Condensed Rings," Interscience Publ., New York, 1951, p. 174.
[6] Erdtman and Robinson, *J.*, 1933, 1530.

could not be cyclised. Diazotisation of the amine gave a good yield of 2 : 3 : 8 : 9-bismethylenedioxy-5 : 6-diazachrysene (IVb). From the mother-liquors of the crystallisation of the nitro-compound (V), an impure material was recovered and subjected to catalytic hydrogenation in benzene solution. Chromatography of the product gave a small amount of compound (Va) and a very small amount of a yellow substance, isomeric with the nitro-compound (V). This is probably the nitro-compound (Vb) which had escaped reduction (for lack of material, its identity could not be confirmed).

Nitration of 2 : 3-methylenedioxy-6-(3 : 4-methylenedioxyphenyl)naphthalene under forced conditions gave a moderate yield of a dinitro-compound which was reduced to a diamine. Cyclisation of its diacetyl derivative gave an acetamidobismethylenedioxymethylbenzophenanthridine, whose ultraviolet spectrum (Fig. 2) was similar to those of the

FIG. 1. FIG. 2. FIG. 3.

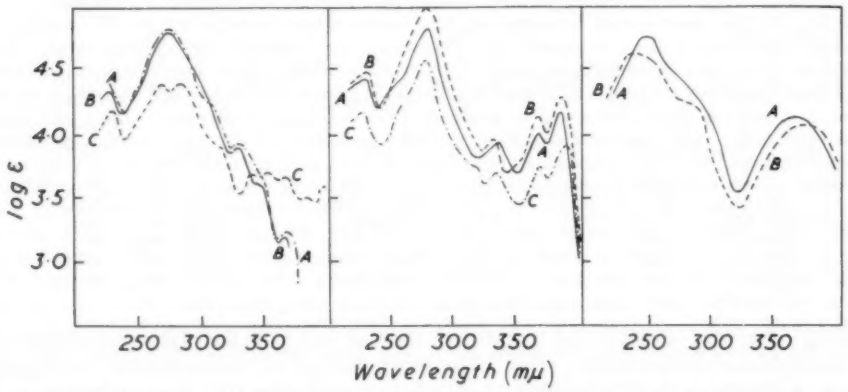


FIG. 1. *Ultraviolet absorption of* (*A*) 2′ : 3′ : 6 : 7-*tetramethoxy- and* (*B*) 2′ : 3′ : 6 : 7-*tetramethoxy*-9-*methyl*-1 : 2-*benzophenanthridine and* (*C*) 2 : 3 : 8 : 9-*tetramethoxy*-5 : 6-*diazachrysene.*

FIG. 2. *Ultraviolet absorption of* (*A*) 2 : 3 : 2′ : 3′-*tetramethoxy-*, (*B*) 2 : 3-2′ : 3′-*bismethylenedioxy-, and* (*C*) 1′(or 4′)-*acetamido*-9-*methyl*-2 : 3-2′ : 3′-*bismethylenedioxy*-7 : 8-*benzophenanthridine.*

FIG. 3. *Ultraviolet absorption of* (*A*) 9 : 10-*dihydro*-2 : 3 : 2′ : 3′-*tetramethoxy*-9 : 10-*dimethyl*-7-8-*dibenzophenanthridine and* (*B*) 9 : 10-*dihydro*-9 : 10-*dimethyl*-2 : 3-2′ : 3′-*bismethylenedioxy*-7 : 8-*dibenzophenanthridine.*

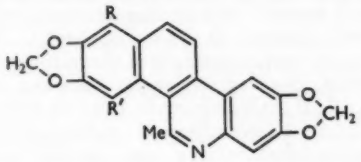
7 : 8-benzophenanthridines (III) and (IIIa), and different from those of the two 1 : 2-benzophenanthridines (II) and (IIa) (Fig. 1). Hydrolysis of this base and deamination yielded the 7 : 8-benzophenanthridine (IIIa), showing thereby that it is an acetamido-9-methyl-2 : 3-2′ : 3′-bismethylenedioxy-7 : 8-benzophenanthridine. One of the nitro-groups in the dinitro-compound must therefore be in the 6′-position. The other cannot be at position 5, since cyclisation should then have yielded a 1 : 2-benzophenanthridine and not a 7 : 8-benzophenanthridine, or at position 2′, since the diacetyl derivative should then have given a mixture of 7 : 8-benzophenanthridines. If positions 7 and 8 are excluded as unlikely, the most probable ones for the second nitro-group are therefore 1 and 4, giving the dinitro-compound structure (VI). The derived diamine is therefore 1-amino-6(or 7)-(6-amino-3 : 4-methylenedioxyphenyl)-2 : 3-methylenedioxynaphthalene (VIa) and the resulting phenanthridine must be 1′(or 4′)-acetamido-9-methyl-2 : 3-2′ : 3′-bismethylenedioxy-7 : 8-benzophenanthridine (VII).

The three 7 : 8-benzophenanthridines (III, IIIa, and VII) whose synthesis and ultraviolet spectra are reported here are of interest because only the parent compound of this group is so far known [7] and its ultraviolet spectrum has not been recorded. The spectra

[7] Graebe, *Annalen*, 1904, **335**, 122.

of members of this group are characteristic and different from those of the 1 : 2-benzophenanthridines. The spectra (Fig. 3) of the dihydro-derivatives obtained by reduction of the quaternary salts of the phenanthridines (III) and (IIIa) also differ remarkably from those reported [2] for similar 1 : 2-benzophenanthridine derivatives.

(VII) R = H, R′ = NH·COMe or *vice versa*.



Experimental

Nitration of 6-(3 : 4-*Dimethoxyphenyl*)-2 : 3-*dimethoxynaphthalene*.—To the naphthalene derivative [1] (5 g.) in acetic acid (20 ml.) cooled in ice–salt and stirred, nitric acid (*d* 1·42; 2·5 ml.) was added during ½ hr. Stirring in ice was continued for 2 hr. and the solid was filtered off and washed with small amounts of acetic acid and with cold alcohol. The dry solid was dissolved in the minimum amount of hot acetic acid and allowed to cool, pale yellow needles (0·2 g.) separating. Recrystallisation from acetic acid yielded greenish-yellow needles of 2-(3 : 4-*dimethoxyphenyl*)-6 : 7-*dimethoxy*-1-*nitronaphthalene*, m. p. 209—210° (Found: C, 64·8; H, 5·2. $C_{20}H_{19}O_6N$ requires C, 65·0; H, 5·1%). The mother-liquor, overnight, deposited reddish crystals. These were redissolved in acetic acid and allowed to cool slowly. A mixture of heavy reddish-yellow prisms and small greenish-yellow needles separated. The latter were washed from the former by small amounts of acetic acid. After two further crystallisations of the yellow needles a further yield (0·6 g.) of the 1-nitronaphthalene, m. p. 209—210°, was obtained. The red solid after two further crystallisations from acetic acid yielded 6-(4 : 5-*dimethoxy*-2-*nitrophenyl*)-2 : 3-*dimethoxynaphthalene* (2·1 g.) as reddish-yellow prisms, m. p. 189—190° (Found: C, 64·7; H, 5·3%).

1-*Amino*-2-(3 : 4-*dimethoxyphenyl*)-6 : 7-*dimethoxynaphthalene*.—The 1-nitro-compound (0·5 g.) in benzene (40 ml.) was reduced catalytically by hydrogen at 50—60 lb./sq. in. after the addition of Adams catalyst (0·2 g.). After 3 hr. the benzene solution was filtered and the catalyst washed several times with benzene. Removal of the solvent yielded the *amine* (0·4 g.), colourless plates (from methanol), m. p. 144—145° (Found: C, 71·0; H, 6·3. $C_{20}H_{21}O_4N$ requires C, 70·8; H, 6·2%). The amine (0·5 g.) in 95% formic acid (2 ml.) was evaporated to dryness and the solid formate heated at 180° for 2 hr. Water was added and the solid obtained washed with dilute hydrochloric acid and water, to yield 1-*formamido*-2-(3 : 4-*dimethoxyphenyl*)-6 : 7-*dimethoxynaphthalene* (0·5 g.) as colourless needles (from ethanol), m. p. 215—216° (Found: C, 68·9; H, 6·0. $C_{21}H_{21}O_5N$ requires C, 68·7; H, 5·7%). The *acetyl derivative* (0·2 g.), prepared from the amine (0·25 g.) by acetic anhydride (5 ml.) in pyridine (0·5 ml.) at 100° for 1 hr., formed colourless needles (from ethanol), m. p. 154—156° (Found: C, 68·9; H, 6·2. $C_{22}H_{23}O_5N$ requires C, 69·3; H, 6·0%).

2′ : 3′ : 6 : 7-*Tetramethoxy*-1 : 2-*benzophenanthridine*.—A solution of the foregoing formamide (0·3 g.) in phosphorus oxychloride (3 ml.) was heated at 100° for 1 hr. After a few minutes a yellow precipitate separated. The excess of phosphorus oxychloride was decomposed with ice-water, the yellow hydrochloride washed with water, then basified with ammonia, and the base recrystallised from pyridine–ethanol to yield 2′ : 3′ : 6 : 7-tetramethoxy-1 : 2-benzophenanthridine (0·2 g.) as colourless plates, m. p. and mixed m. p. (cf. ref. 2) 305—306° (Found: C, 72·6; H, 5·4; N, 4·2. Calc. for $C_{21}H_{19}O_4N$: C, 72·2; H, 5·5; N, 4·0%).

2′ : 3′ : 6 : 7-*Tetramethoxy*-9-*methyl*-1 : 2-*benzophenanthridine*.—The above acetamide (0·2 g.) and phosphorus oxychloride (3 ml.) heated at 100° for 2 hr. yielded, as above, 2′ : 3′ : 6 : 7-*tetramethoxy*-9-*methyl*-1 : 2-*benzophenanthridine* (0·15 g.), m. p. 275—276° (from pyridine–ethanol) (Found: C, 72·6; H, 5·6. $C_{22}H_{21}O_4N$ requires C, 72·7; H, 5·8%).

6-(2-*Amino*-4 : 5-*dimethoxyphenyl*)-2 : 3-*dimethoxynaphthalene*.—The 2′-nitro-compound (1·0 g.) was hydrogenated in benzene (50 ml.) during 3 hr. at 55—60 lb. after addition of Adams catalyst (0·2 g.). Working up as before yielded the *amine* (0·9 g.) as almost colourless prisms (from ethanol), m. p. 201—202° (Found: C, 70·5; H, 6·2%), yielding as before the *formyl derivative* (0·25 g. from 0·3 g.) as colourless needles (from ethanol), m. p. 206—207° (Found:

C, 69·3; H, 5·8%), which was not cyclised by phosphorus oxychloride; the *acetyl derivative* (0·4 g. from 0·5 g.) formed colourless needles (from dioxan), m. p. 204—205° (Found: C, 69·7; H, 6·2%).

2 : 3 : 2′ : 3′-*Tetramethoxy*-9-*methyl*-7 : 8-*benzophenanthridine*.—The above acetyl derivative (0·3 g.) in phosphorus oxychloride (5 ml.) at 100° for 2 hr. yielded, as before, 2 : 3 : 2′ : 3′-*tetramethoxy*-9-*methyl*-7 : 8-*benzophenanthridine* (0·2 g.) as needles (from pyridine–ethanol), m. p. 259—260° (Found: C, 72·8; H, 5·9%). The methosulphate, m. p. 248—250° (decomp.) (prepared by methyl sulphate in hot nitrobenzene) on reduction with lithium aluminium hydride gave the 9 : 10-*dihydro*-10-*methyl derivative*, m. p. 184—185° (from alcohol) (Found: C, 72·2; H, 6·2. $C_{23}H_{25}O_4N$ requires C, 72·8; H, 6·6%).

2 : 3 : 8 : 9-*Tetramethoxy*-5 : 6-*diazachrysene*.—6-(2-Amino-4 : 5-dimethoxyphenyl)-2 : 3-dimethoxynaphthalene (0·2 g.) was dissolved in 48% hydrobromic acid (10 ml.), cooled in ice–salt, and treated dropwise with stirring with sodium nitrite (0·2 g.) in water (5 ml.). Stirring was continued for ½ hr., and to the cold solution was then added with stirring freshly precipitated copper (1·0 g.). The mixture was allowed to rise slowly to room temperature and left overnight. The solid which separated was filtered off and extracted repeatedly with hot chloroform. The chloroform solution was washed with dilute aqueous sodium hydroxide, then with water. The dried (Na_2SO_4) extracts yielded on evaporation a red solid which was washed with cold alcohol and crystallised from acetic acid, to yield yellow 2 : 3 : 8 : 9-*tetramethoxy*-5 : 6-*diazachrysene* (0·04 g.) which blackened at 250° and did not melt at 360° (Found: C, 68·2; H, 5·4; N, 7·4. $C_{20}H_{18}O_4N_2$ requires C, 68·5; H, 5·1; N, 8·0%). Use of cuprous bromide in hydrobromic acid in place of copper led to the same result.

2 : 3-*Methylenedioxy*-6-(4 : 5-*methylenedioxy*-2-*nitrophenyl*)*naphthalene*.—A suspension of 2 : 3-methylenedioxy-6-(3 : 4-methylenedioxyphenyl)naphthalene [1] (2 g.) in acetic acid (10 ml.) was treated at 20—25° with stirring with fuming nitric acid (*d* 1·48; 1 ml.). The naphthalene dissolved but soon a yellow precipitate separated. The mixture was allowed to come to room temperature and stirring continued for 2 hr. The product was filtered off and washed first with a little acetic acid and then with alcohol. One crystallisation from acetic acid yielded yellow crystals, m. p. 220—227°. Two further crystallisations yielded the *nitro-compound* (0·7 g.) as brownish-yellow needles (from acetic acid), m. p. 241—242° (Found: C, 63·9; H, 3·1. $C_{18}H_{11}O_6N$ requires C, 64·1; H, 3·3%). The mother-liquors from crystallisations were diluted with water, and the yellow solid (0·7 g.; m. p. 185—230°) filtered off. It was dissolved in benzene (50 ml.) and hydrogenated at 55—60 lb. for 3 hr. after addition of Adams catalyst (0·2 g.). Working up yielded a yellow solid which was chromatographed over alumina. The yellow band which came down first yielded on evaporation a solid, m. p. 220—225° giving, on two crystallisations, yellow cubes of a *nitro-compound* (0·05 g.), m. p. 225—227° (from ethanol–acetic acid) (Found: C, 64·4; H, 3·2%). The mixed m. p. with the 2′-nitrophenyl isomer was 190—200°. Subsequent fractions yielded a basic solid which after acetylation and crystallisation from ethanol yielded 6-(2-acetamido-4 : 5-methylenedioxyphenyl)-2 : 3-methylenedioxynaphthalene (see below), m. p. and mixed m. p. 204—205°.

6-(2-*Amino*-4 : 5-*methylenedioxyphenyl*)-2 : 3-*methylenedioxynaphthalene*.—The nitro-compound (0·5 g.) was reduced in benzene (100 ml.) at a hydrogen pressure of 55—60 lb. after the addition of Adams catalyst (0·2 g.). Working up gave the *amine* (0·3 g.) as colourless plates (from ethanol), m. p. 201—202° (Found: C, 70·1; H, 4·4. $C_{18}H_{13}O_4N$ requires C, 70·4; H, 4·2%), yielding with formic acid a *formyl derivative* as needles (from ethanol), m. p. 160° (Found: C, 68·3; H, 4·2. $C_{19}H_{13}O_5N$ requires C, 68·1; H, 3·9%) (which could not be cyclised), and with acetic anhydride an *acetyl derivative*, needles (from ethanol), m. p. 204—205° (Found: C, 69·3; H, 4·7. $C_{20}H_{15}O_5N$ requires C, 68·8; H, 4·3%).

9-*Methyl*-2 : 3-2′ : 3′-*bismethylenedioxy*-7 : 8-*benzophenanthridine*.—The above acetamide (0·2 g.) and phosphorus oxychloride (2 ml.), heated at 100° for 2 hr., yielded 9-*methyl*-2 : 3-2′ : 3′-*bismethylenedioxy*-7 : 8-*benzophenanthridine* (0·1 g.), colourless needles (from pyridine–ethanol), m. p. 293—294° (decomp.) (Found: C, 72·8; H, 4·3. $C_{20}H_{13}O_4N$ requires C, 72·5; H, 3·9%). The methosulphate, m. p. 307—310° (decomp.) (prepared by methyl sulphate in hot nitrobenzene), on reduction with lithium aluminium hydride, yielded the yellow 9 : 10-*dihydro*-10-*methyl derivative*, m. p. 209—210° (from benzene–ethanol) (Found: C, 72·4; H, 4·9. $C_{21}H_{17}O_4N$ requires C, 72·6; H, 4·9%).

2 : 3-8 : 9-*Bismethylenedioxy*-5 : 6-*diazachrysene*.—6-(2-Amino-4 : 5-methylenedioxyphenyl)-2 : 3-methylenedioxynaphthalene (0·1 g.) in acetic acid (2·5 ml.) and concentrated hydrochloric

acid (0·5 ml.) was cooled to 0° and diazotised with a solution of sodium nitrite (0·2 g. in water, 2 ml.). The diazonium solution was allowed to rise slowly to room temperature and left overnight. Water was added and the brown solid centrifuged off and washed with water, dilute sodium hydroxide, and finally boiling water, yielding 2 : 3-8 : 9-*bismethylenedioxy*-5 : 6-*diazachrysene* (0·04 g.) as brown needles (from nitrobenzene), which did not melt at 360° (Found: C, 68·2; H, 2·8; N, 8·7. $C_{18}H_{10}O_4N_2$ requires C, 67·9; H, 3·1; N, 8·8%).

2 : 3-*Methylenedioxy*-6(or 7)-(4 : 5-*methylenedioxy*-2-*nitrophenyl*)-1-*nitronaphthalene*.—2 : 3-Methylenedioxy-6-(3 : 4-methylenedioxyphenyl)naphthalene (2 g.), suspended in acetic acid (20 ml.), was treated at 25—30° with nitric acid (*d* 1·48; 4 ml.), with stirring. The naphthalene dissolved but soon a yellow precipitate separated. After 2 hours' stirring at room temperature, the temperature was slowly raised to 60—70° and kept there for 3 hr. The yellow powder which separated was filtered off and washed with acetic acid and then alcohol. The dry solid was twice crystallised from a large volume of acetic acid, to yield the yellow *dinitro-derivative* (0·5 g.), m. p. 286—287° (decomp.) (Found: C, 56·3; H, 2·5. $C_{18}H_{10}O_8N_2$ requires C, 56·5; H, 2·6%).

1-*Amino*-6(or 7)-(2-*amino*-4 : 5-*methylenedioxyphenyl*)-2 : 3-*methylenedioxynaphthalene*.—The foregoing dinitro-compound (0·5 g.), suspended in benzene (70 ml.), was shaken for 3 hr. in hydrogen at 60 lb. after addition of Adams catalyst (0·2 g.). The solid dissolved and the solution became almost colourless. Working up yielded the *diamine* (0·35 g.) as pale brown plates (from ethanol), m. p. 177—178° (Found: C, 67·5; H, 4·6. $C_{18}H_{14}O_4N_2$ requires C, 67·1; H, 4·4%), yielding with formic acid as before a *diformyl derivative* (0·4 g. from 0·5 g.) as colourless crystals (from pyridine–ethanol), m. p. 330° (decomp.) (Found: C, 63·7; H, 4·2. $C_{20}H_{14}O_6N_2$ requires C, 63·2; H, 3·7%), which was not cyclised. The *diacetyl derivative* (1 g. from 1 g.) formed colourless feathery crystals (from pyridine), m. p. 342—343° (decomp.) (Found: C, 65·5; H, 4·6. $C_{22}H_{18}O_6N_2$ requires C, 65·0; H, 4·4%).

1′(*or* 4′)-*Acetamido*-9-*methyl*-2 : 3-2′ : 3′-*bismethylenedioxy*-7 : 8-*benzophenanthridine*.—The foregoing diacetamide (1 g.) and phosphorus oxychloride (5 ml.) were heated together at 100° for 3 hr. The reactant slowly dissolved to a yellow solution with an intense green fluorescence. Working up yielded the *benzophenanthridine* (0·6 g.) as colourless needles (from pyridine–ethanol), m. p. 329—330° (decomp.) (Found: C, 68·5; H, 4·6. $C_{22}H_{16}O_5N_2$ requires C, 68·1; H, 4·1%).

1′(*or* 4′)-*Amino*-9-*methyl*-2 : 3-2′ : 3′-*bismethylenedioxy*-7 : 8-*benzophenanthridine*.—The foregoing acetamidophenanthridine (0·1 g.), ethanol (10 ml.), and concentrated hydrochloric acid (20 ml.) were heated together under reflux for 6 hr. After 3 hr. a further 10 ml. of concentrated hydrochloric acid were added. The original lemon-yellow hydrochloride changed to a fluffy pale yellow solid. The solid was filtered off, washed with a small quantity of alcohol, and basified with ammonia. The pale yellow solid obtained yielded on crystallisation the *aminobenzophenanthridine* (0·06 g.) as pale yellow needles (from pyridine–ethanol), m. p. 281—282° (decomp.) (Found: C, 69·0; H, 4·3. $C_{20}H_{14}O_4N_2$ requires C, 69·4; H, 4·0%).

Deamination of 1′(*or* 4′)-*Amino*-9-*methyl*-2 : 3-2′ : 3′-*bismethylenedioxy*-7 : 8-*benzophenanthridine*.—The preceding amino-compound (0·1 g.) was suspended in water (20 ml.) containing concentrated sulphuric acid (*d* 1·84; 5 ml.), cooled to 0°, and diazotised with sodium nitrite (0·2 g.) in water (5 ml.). The solid gradually went into solution. After ½ hour's stirring 35% hypophosphorous acid (10 ml.) was added in small lots at <0—10°. The mixture was then allowed slowly to reach room temperature. After 1 hr. a yellow precipitate began to separate. Next morning the yellow solid was filtered off, washed with water, and basified with sodium hydroxide solution. The pale brown precipitate was washed with water and crystallised from pyridine–ethanol, yielding 9-methyl-2 : 3-2′ : 3′-bismethylenedioxy-7 : 8-benzophenanthridine (0·06 g.), colourless needles, m. p. and mixed m. p. 293—294° (Found: C, 72·3; H, 4·2%).

We thank Dr. A. S. Bailey for a gift of the benzophenanthridine (II), Mr. S. Selvavinayagam for the microanalyses, and the Government of India for the award of a studentship (K. W. G.).

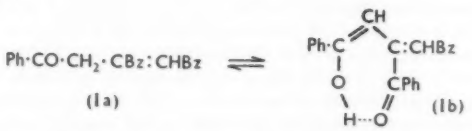
PRESIDENCY COLLEGE, MADRAS, INDIA. [*Received, August 26th,* 1957.]

89. *Structure and Synthesis of Kostanecki's Compound, m. p.* 120°.

By P. F. Devitt, (Mrs.) E. M. Philbin, and T. S. Wheeler.

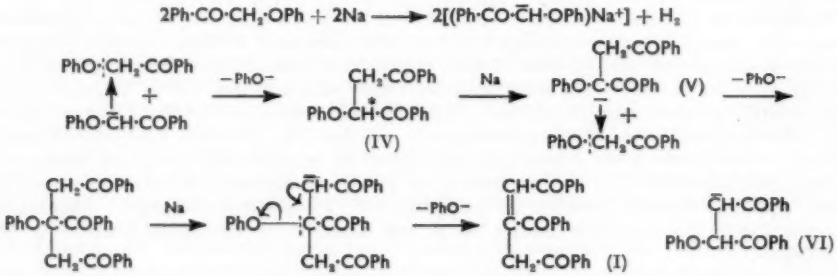
The substance $(C_8H_6O)_x$ obtained by the base-catalysed self-condensation of ω-phenoxyacetophenone is 1 : 2 : 3-tribenzoylpropene. An unambiguous synthesis of this olefin is provided by the action of bromine on 1 : 2 : 3-tribenzoylpropane.

Kostanecki and Tambor [1] were unable to assign a structure to an orange compound $(C_8H_6O)_x$ (I), m. p. 120°, which they obtained by the sodium-catalysed condensation of ω-phenoxyacetophenone. It has now been found that this substance is also obtained by base-condensation of ω-*p*-chlorophenoxyacetophenone, so that the aryloxy-group is eliminated in the reaction. Further, as Kostanecki and Tambor [1] showed, the orange compound (I) can be reduced to a colourless product which has now been identified as 1 : 2 : 3-tribenzoylpropane, $CHBz(CH_2Bz)_2$, previously obtained by Lutz and Palmer [2] from acetophenone and dibenzoylethylene. Treatment of the triketone with bromine yielded an unstable bromo-compound which lost hydrogen bromide with production of the orange compound (I). This reaction constitutes an unambiguous synthesis of Kostanecki's compound.



Compound (I) is, accordingly, 1 : 2 : 3-tribenzoylpropene. As the enol form (Ib), it formed monomethyl and monoacyl derivatives, Ph·C(OR):CH·CBz:CHBz (III; R = Me or acyl). Infrared spectra confirmed the structure (I) (cf. Table). The ultraviolet absorption maximum in ethanol for compound (I) (257 mμ) showed a bathochromic shift as compared with the maxima for acetophenone (240 mμ) and ω-phenoxyacetophenone (243 mμ).

A possible alternative to the condensation mechanism suggested by Yates and his colleagues [3] is:



It is assumed that the compound (IV) reacts with sodium to give the ion (V) rather than (VI). The phenoxyl group is electrophilic so that the hydrogen atom (H*) in (IV) is the more likely to be replaced.

The reaction is not general since no useful result was obtained in attempts to condense

[1] Kostanecki and Tambor, *Ber.*, 1902, **35**, 1679.
[2] Lutz and Palmer, *J. Amer. Chem. Soc.*, 1935, **57**, 1952.
[3] Yates, Farnum, and Stout, *Chem. and Ind.*, 1956, 821.

ω-hydroxyacetophenone, ω-phenoxy-*p*-phenylacetophenone, or *p*-bromo-ω-phenoxyacetophenone in the presence of sodamide. 1 : 2-Di-*p*-bromobenzoylethane [4] was an unexpected by-product in the preparation of the last compound from *p*ω-dibromoacetophenone and phenol.

Infrared bands (cm.$^{-1}$).

1 : 2 : 3-Tribenzoylpropene in KBr	
Conjug. C:O	1622
C:C·C:O or CO·C[CH:C(OH)]:C·C:O	1596, 1578(s), 1534—1528(s)
CO·CH_2	1416
Ph, probably monosubst.	1490, 1451, 1179(s), 1051(s), 962(s), 761(s), 680(s)

p-NO_2·C_6H_4·CO·O·CPh:CH·CBz:CHBz in $CHCl_3$	
Conjug. C:O	1665, 1647
CO·O·C:C	1742(s)
NO_2 (probably incl. conjug. C:C)	1556(s), 1345(s)
p-NO_2·C_6H_4·CO·O	1276, 1230(s), 1072(s)
p-Disubstn.	780, 690(s)

1 : 2 : 3-Tribenzoylpropene in $CHCl_3$	
Conjug. C:O	1666(s) (sh 1682)
C:C·C:O	1597, 1578
Assoc. OH (probably H-bonded)	3556(w)
Ph	1485, 1450

Experimental

Crystallisation was from ethanol unless otherwise stated.

1 : 2 : 3-*Tribenzoylpropene*.—A stirred solution of ω-phenoxyacetophenone (10 g.) in xylene (70 ml.) was treated with granulated sodium (1 g.) and kept at 50° until dissolution of the metal was complete. The mixture was acidified with acetic acid and treated with ether. 1 : 2 : 3-*Tribenzoylpropene* was extracted from the non-aqueous layer by dilute aqueous sodium hydroxide from which it was precipitated by carbon dioxide. It crystallised in orange needles (1 g.), m. p. 121—123° (Found: C, 81·1; H, 5·3. $C_{24}H_{18}O_3$ requires C, 81·3; H, 5·1%). Kostanecki and Tambor [1] gave m. p. 120° for their " orange " compound.

A mixture of ω-*p*-chlorophenoxyacetophenone [5] (13 g.), ether (200 ml.), powdered sodamide [3] (4·3 g.), and methanol (2 drops) was refluxed for 2 hr. under nitrogen. 1 : 2 : 3-Tribenzoylpropene (mixed m. p. confirmation) was recovered from the acidified product as described above. The yield of crystallised material was 2·2 g.

Bromine (0·5 g.) in glacial acetic acid (5 ml.) was added dropwise with stirring to a cooled suspension of 1 : 2 : 3-tribenzoylpropane [2] (1 g.) in the same solvent (10 ml.). 1 : 2 : 3-Tribenzoylpropene (mixed m. p.; yield of crystallised product, 0·1 g.) was precipitated when the mixture was warmed and added to water.

Reduction of 1 : 2 : 3-*Tribenzoylpropene*.—A mixture of the tribenzoylpropene (1 g.), ethanol (10 ml.), and sodium dithionite (0·6 g.) was refluxed for 2 hr. and filtered. The filtrate was acidified with glacial acetic acid and diluted with water to turbidity. 1 : 2 : 3-Tribenzoylpropane, which separated on cooling, formed prisms (0·8 g.), m. p. and mixed m. p. with an authentic specimen [2] 124—125° (Found: C, 81·2; H, 5·7. Calc. for $C_{24}H_{20}O_3$: C, 80·9; H, 5·7%). The reduction was also effected by zinc and dilute ethanolic acetic acid.[6]

Tribenzoylpropene with dimethyl sulphate and aqueous sodium hydroxide furnished 3 : 4-*dibenzoyl*-1-*methoxy*-1-*phenylbutadiene* (III; R = Me), yellow needles, m. p. 166° (Found: C, 81·7; H, 5·6; OMe, 8·6. $C_{25}H_{20}O_3$ requires C, 81·5; H, 5·5; OMe, 8·4%). The propene derivatives with pyridine and benzoyl chloride gave 3 : 4-*dibenzoyl*-1-*benzoyloxy*-1-*phenylbutadiene* (III; R = Bz) which was insoluble in the usual solvents. It was purified by washing it with boiling ethanol and was obtained in grey crystals, m. p. 212° (Found: C, 81·4; H, 4·7. $C_{31}H_{22}O_4$ requires C, 81·2; H, 4·8%). 3 : 4-*Dibenzoyl*-1-p-*nitrobenzoyloxy*-1-*phenylbutadiene* (III; R = *p*-nitrobenzoyl), crystallised in needles, m. p. 207° (Found: C, 74·4; H, 4·1; N, 3·1. $C_{31}H_{21}O_6N$ requires C, 74·0; H, 4·2; N, 2·8%). 3 : 4-*Dibenzoyl*-1-*furoyloxy*-1-*phenylbutadiene* (III; R = furoyl) formed yellowish-brown crystals, m. p. 158—160° (Found: C, 78·1; H, 4·5. $C_{29}H_{20}O_5$ requires C, 77·7; H, 4·5%).

ω-*Phenoxy*-p-*phenylacetophenone*, which crystallised in plates, m. p. 91° (Found: C, 83·3;

[4] Conant and Lutz, *J. Amer. Chem. Soc.*, 1925, **47**, 891.
[5] Wright and Lincoln, *ibid.*, 1952, **74**, 6301.
[6] Cf. Iyer, Shah, and Venkataraman, *Proc. Indian Acad. Sci.*, 1951, **33**, *A*, 120.

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H, 5·7. $C_{20}H_{16}O_2$ requires C, 83·3; H, 5·5%), was prepared from ω-bromo-*p*-phenylacetophenone [7] and phenol in aqueous sodium hydroxide.[8]

1 : 2-*Di*-p-*bromobenzoylethane and* p-*Bromo*-ω-*phenoxyacetophenone*.—A mixture of *p*ω-dibromoacetophenone [9] (75 g.), phenol (26 g.) and 10% aqueous sodium hydroxide (100 ml.) was refluxed for 3 hr. Fractional crystallisation of the solid product from glacial acetic acid gave a first crop of 1 : 2-di-*p*-bromobenzoylethane which separated in plates (3 g.), m. p. 182°, not depressed by the addition of an authentic sample [4] (Found: C, 48·4; H, 2·9. Calc. for $C_{16}H_{12}O_2Br_2$: C, 48·5; H, 3·0%). The *bis*-2 : 4-*dinitrophenylhydrazone* formed orange crystals, m. p. 248—250° (decomp.) (Found: C, 43·9; H, 2·9; H, 14·5; Br, 20·8. $C_{28}H_{20}O_8N_8Br_2$ requires C, 44·4; H, 2·6; N, 14·9; Br, 21·2%).

The second crop (p-*bromo*-ω-*phenoxyacetophenone*) separated in needles (48 g.), which on further crystallisation had m. p. 90—91° (Found: C, 57·7; H, 3·8; Br, 27·7. $C_{14}H_{11}O_2Br$ requires C, 57·7; H, 3·8; Br, 27·5%).

Professor Peter Yates and his colleagues [3] arrived independently at the structure of Kostanecki's compound. We acknowledge their priority in obtaining confirmatory evidence. We appreciate their agreement to simultaneous publication of preliminary notes.[3, 10]

One of us (P. F. D.) thanks Dr. Michael J. Walsh and University College, Dublin, for the award of a Michael J. Walsh Research Fellowship. Grateful acknowledgment is also made to Professor Hs. H. Günthard, Eidg. Technische Hochschule, Zürich, and Professor Wesley Cocker and Mr. E. R. Stuart, Trinity College, Dublin, for providing the infrared determinations and assisting in their interpretation. The authors also thank a Referee for valuable suggestions relative to the reaction mechanism discussed in this paper.

UNIVERSITY COLLEGE, DUBLIN. [*Received, September 18th*, 1957.]

[7] Carpenter and Turner, *J. Chem. Soc.*, 1934, 869.
[8] Möhlau, *Ber.*, 1882, **15**, 2497.
[9] Langley, *Org. Synth.*, 1946, Coll. Vol. I, p. 127.
[10] Devitt, Philbin, and Wheeler, *Chem. and Ind.*, 1956, 822.

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90. *Reactions of Halogenobistrifluoromethylphosphines with Amines and Ammonia; and their Behaviour with Phosphine and Hydrogen Sulphide.*[1]

By G. S. HARRIS.

An investigation of the reactions of chlorobistrifluoromethylphosphine with ammonia, methylamine, dimethylamine, and aniline has led to the isolation of four new phosphorus–nitrogen compounds, $(CF_3)_2P{\cdot}NH_2$, $(CF_3)_2P{\cdot}NHMe$, $(CF_3)_2P{\cdot}NMe_2$, and $(CF_3)_2P{\cdot}NHPh$. The properties and reactions of these compounds have been studied and their infrared spectra recorded.

Halogenobistrifluoromethylphosphines with phosphine and hydrogen sulphide did not give rise to any new compounds.

INTERACTION of phosphorus and trifluoroiodomethane at 200—220° yields tristrifluoromethylphosphine, iodobistrifluoromethylphosphine, and di-iodotrifluoromethylphosphine, together with phosphorus iodides.[2] Interest in the iodotrifluoromethylphosphines has, till now, been confined to determination of their simple physical properties and their use in the preparation of the series of compounds in which the iodine atoms are replaced by other halogens or pseudo-halogens; [2] also, a detailed study of their hydrolysis has been made in connection with the preparation of trifluoromethylphosphorus oxy-acids.[3, 4] Recently, Mahler and Burg [5] have used di-iodotrifluoromethylphosphine as starting material for the preparation of the compound $(CF_3{\cdot}P)_4$. Comparison of the properties and

[1] Preliminary publication, Harris, *Proc. Chem. Soc.*, 1957, 118.
[2] Bennett, Emeléus, and Haszeldine, *J.*, 1953, 1565.
[3] *Idem*, *J.*, 1954, 3598.
[4] *Idem*, *J.*, 1954, 3896.
[5] Mahler and Burg, *J. Amer. Chem. Soc.*, 1957, **79**, 251.

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reactions of these halogenotrifluoromethylphosphines with those of other organohalogenophosphines and simple phosphorus trihalides would seem to be a useful study and the work described in this paper represents the results of the first stages of such an investigation.

Numerous products have been obtained by reaction of halogenophosphines with amines;[6] but frequently they are not those to be expected if the interaction simply involved elimination of hydrogen halide. Iminophosphines are often formed and usually the reactions result in a mixture of products. Reaction of ammonia with halogenophosphines does not appear to have been reported and no aminophosphines of the type $R_2P{\cdot}NH_2$ have been described. Phosphorus trihalides, on the other hand, are said to react with liquid ammonia to yield triaminophosphine which loses ammonia on warming to 0° with the formation of condensed phosphorus–nitrogen products.[7]

Dihalogenophosphines and phosphine have been shown to interact by the elimination of hydrogen chloride,[8] giving a product of uncertain structure and, similarly, hydrogen sulphide reacts in a complex manner with dihalogenophosphines to give a mixture of phosphorus thio-acids.[9]

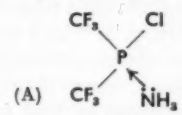
It was thought of interest to study analogous reactions involving halogenotrifluoromethylphosphines to discover the effect of the strongly electronegative trifluoromethyl groups on the course of the reactions and on the nature and stability of the products. This communication describes the results of an investigation of some reactions of chloro- and iodo-bistrifluoromethylphosphine.

Chlorobistrifluoromethylphosphine and ammonia in the vapour phase produce good yields of aminobistrifluoromethylphosphine and ammonium chloride, according to the equation:

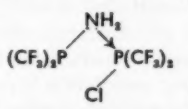
$$(CF_3)_2PCl + 2NH_3 \longrightarrow (CF_3)_2P{\cdot}NH_2 + NH_4Cl \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

and the same products are obtained in the liquid phase.

It was not possible, by increasing the ratio of halogenophosphine to ammonia in the vapour-phase reaction, to obtain a compound with more than one hydrogen atom of ammonia replaced by the $(CF_3)_2P-$ group. This is not unexpected if the first stage of the reaction [equation (1)] involves the intermediate (A) which loses hydrogen chloride to give $(CF_3)_2P{\cdot}NH_2$. This molecule does not react with more $(CF_3)_2PCl$ since the strong electron-attracting influence of the trifluoromethyl groups diminishes the availability of electrons on the nitrogen atom for donation to the phosphorus of another chlorobistrifluoromethylphosphine molecule, so that the intermediate complex (B) is not formed.



(A)



(B)

It seems likely that the nitrogen lone pair in aminobistrifluoromethylphosphine will take part in π-bonding with the 3*d*-orbital of the phosphorus atom; that is, a d_π–p_π bond[10] is probably formed which could account for the unusual stability of the molecule. Mahler and Burg[5] have suggested that the stability of the four-membered phosphorus ring in $(CF_3{\cdot}P)_4$ is due to a similar type of "extra-bonding."

An alternative but less satisfactory method for preparing aminobistrifluoromethylphosphine is by the interaction of tristrifluoromethylphosphine and liquid ammonia at about −70°, when the main reaction taking place is the slow ammonolysis:

$$(CF_3)_3P + NH_3 \longrightarrow (CF_3)_2P{\cdot}NH_2 + CHF_3$$

[6] See Kosolapoff, "Organophosphorus Compounds," Wiley, New York, 1950, p. 300, for a list of compounds.
[7] Hugot, *Compt. rend.*, 1905, **141**, 1235.
[8] Michaelis, *Ber.*, 1875, **8**, 499.
[9] Kosolapoff, *op. cit.*
[10] Craig, Maccoll, Nyholm, Orgel, and Sutton, *J.*, 1954, 332.

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From the reaction mixture a material of low volatility was also isolated, possibly a product of further ammonolysis of the CF_3–P bond in aminobistrifluoromethylphosphine. It is noteworthy that tristrifluoromethylphosphine is not hydrolysed by water, even at 100°.[2]

Aminobistrifluoromethylphosphine is not obtained when iodobistrifluoromethylphosphine and sodamide are allowed to interact: $(CF_3)_2PI + NaNH_2 \not\longrightarrow (CF_3)_2P{\cdot}NH_2 +$ NaI. This contrasts with the behaviour of phosphorus halides, which react readily with sodamide.[11]

The vapour-phase reactions of chlorobistrifluoromethylphosphine with methylamine and dimethylamine follow a similar course to (1) above, yielding methylaminobistrifluoromethylphosphine, $(CF_3)_2P{\cdot}NHMe$, and dimethylaminobistrifluoromethylphosphine, $(CF_3)_2P{\cdot}NMe_2$, respectively. Phenylaminobistrifluoromethylphosphine, $(CF_3)_2P{\cdot}NHPh$, has been obtained by the reaction of aniline and chlorobistrifluoromethylphosphine in the liquid phase.

When iodobistrifluoromethylphosphine and phosphine are mixed in the gas phase (at *ca.* 300 mm. and 20°) crystals of phosphonium iodide and phosphorus di-iodide are slowly deposited and the iodophosphine is reduced to bistrifluoromethylphosphine. The same reaction appears to occur in the liquid phase and no evidence was obtained for the formation of a compound containing a P–P link.

Chlorobistrifluoromethylphosphine and hydrogen sulphide do not react in the vapour (at 15 mm. and 25°) or liquid phase.

Dihalogenotrifluoromethylphosphines react readily with ammonia and amines; the products are being investigated.

The four aminotrifluoromethylphosphines obtained are colourless liquids. Their melting points (±0·5°) were determined directly, and boiling points have been obtained by extrapolation of the vapour pressure–temperature graphs which are straight lines expressible by the general formula $\log_{10} p_{mm.} = AT^{-1} + B$ (see Table).

Compound	M. p.	B. p.	*A*	*B*	Latent heat of vaporn. (cal. mole^{-1})	Trouton's constant
$(CF_3)_2P{\cdot}NH_2$	−87·6°	67·1°	−1872	8·398	8565	25·20
$(CF_3)_2P{\cdot}NHMe$	−46·5	73·2	−1890	8·336	8650	24·98
$(CF_3)_2P{\cdot}NMe_2$	−81·5	83·2	−1698	7·651	7771	21·80
$(CF_3)_2P{\cdot}NHPh$	+ 1·7	182·1	−2183	7·658	9991	21·96

Aminobistrifluoromethylphosphine is considerably less volatile than tristrifluoromethylphosphine (b. p. 17°) and chlorobistrifluoromethylphosphine (b. p. 21°), and the abnormally high values of Trouton's constant for this compound and methylaminobistrifluoromethylphosphine suggest that association is present in the liquid phase, due to hydrogen bonding.

Aminobistrifluoromethylphosphine is unaffected by the action of heat *in vacuo* (in a Pyrex glass tube) up to 250°, but above this temperature decomposition begins and among the products identified are fluoroform, phosphorus fluorides, nitrogen, hydrogen cyanide (and silicon tetrafluoride).

The aminophosphines described are all unstable to hydrolytic agents and these bring about rupture of the P–N bond as well as one or both of the P–C bonds. Aminobistrifluoromethylphosphine is hydrolysed by water and dilute acid at 20°, liberating 1 mol. of fluoroform:

$$(CF_3)_2P{\cdot}NH_2 + 2H_2O \longrightarrow CF_3{\cdot}PHO{\cdot}ONH_4 + CHF_3$$

$$(CF_3)_2P{\cdot}NH_2 + HCl + 2H_2O \longrightarrow CF_3{\cdot}PHO{\cdot}OH + NH_4Cl + CHF_3$$

Alkaline hydrolysis at 20° removes the two trifluoromethyl groups quantitatively as fluoroform and the amino-group as ammonia:

$$(CF_3)_2P{\cdot}NH_2 + 2NaOH + H_2O \longrightarrow Na_2HPO_3 + NH_3 + 2CHF_3$$

[11] Winter, *J. Amer. Chem. Soc.*, 1904, **26**, 1484.

The other aminophosphines of the series undergo similar alkaline hydrolysis at 80—100°, but their reaction with water at 20° is not quantitative except in the case of phenylaminobistrifluoromethylphosphine which reacts like aminobistrifluoromethylphosphine, giving 1 mol. of fluoroform.

Hydrogen chloride reacts with aminobistrifluoromethylphosphine through attack on the phosphorus–nitrogen bond, to give chlorobistrifluoromethylphosphine and ammonium chloride:

$$(CF_3)_2P{\cdot}NH_2 + 2HCl \longrightarrow (CF_3)_2PCl + NH_4Cl$$

and the reaction of aminobistrifluoromethylphosphine with chlorine also results in breakage of the phosphorus–nitrogen link; but it is more complex and yields ammonium chloride and a slightly volatile liquid which is probably a mixture of the addition compound $(CF_3)_2P{\cdot}NH_2{,}Cl_2$ and bistrifluoromethylphosphorus trichloride, $(CF_3)_2PCl_3$; a trace of chlorotrifluoromethane is also produced.

The composition of the molecule $(CF_3)_2P{\cdot}NH_2$ suggests that the hydrogen atoms attached to nitrogen may be acidic [compare the behaviour of sulphamide which forms a silver salt $(Ag{\cdot}NH)_2SO_2$]. However, attempts to prepare the salt $(CF_3)_2P{\cdot}NHM$ (M = Ag, Na) were not successful and the only evidence for acidic character of the hydrogens is that solutions of aminobistrifluoromethylphosphine in pyridine are better electrolytes than the pure solvent ($\kappa_{solv.} = 1{\cdot}07 \times 10^{-6}$ ohm^{-1} cm.$^{-1}$; $\kappa_{soln.} = 5{\cdot}6 \times 10^{-6}$ ohm^{-1} cm.$^{-1}$; $\Lambda_m = 0{\cdot}03$ ohm^{-1} cm.^{2} mole^{-1}) and this might conceivably be due to the presence in the solution of $[(CF_3)_2P{\cdot}NH^-][C_5H_5{\cdot}NH^+]$ ion-pairs. In the same connection it was found that dimethylaminobistrifluoromethylphosphine did not form a quaternary salt with methyl iodide and this seems to indicate the absence of basic character of the nitrogen atom in these compounds.

The infrared absorption spectra of the aminophosphines, $(CF_3)_2P{\cdot}NH_2$, $(CF_3)_2P{\cdot}NHMe$, $(CF_3)_2P{\cdot}NMe_2$, and $(CF_3)_2P{\cdot}NHPh$, are useful for characterisation (cf. p. 519). The nitrogen–hydrogen stretching vibrations lie in the region 3350—3490 cm.$^{-1}$, and the NH_2 deformation is represented by one band at 1569 cm.$^{-1}$. Carbon–fluorine stretching lies between 1210 and 1100 cm.$^{-1}$ and there are three strong maxima in each case [cf. Bennett, Emeléus, and Haszeldine [2] who report that trifluoromethylphosphorus derivatives of the type $(CF_3)_2PX$ (X = I, CN) have three main maxima in this region]. Each compound has one band in the region 730—750 cm.$^{-1}$ and this is probably a trifluoromethyl deformation frequency.[2,4] The absorption bands due to the *N*-alkyl and *N*-aryl groups in these compounds are at the usual frequencies. It is not possible to assign with certainty absorption due to phosphorus–nitrogen stretching in the spectra of these compounds (Corbridge [12] gives 750—680 cm.$^{-1}$ as the region for phosphorus–nitrogen stretching). In the simplest member of the series, aminobistrifluoromethylphosphine, two strong bands appear between the carbon–fluorine stretching absorption (1115 cm.$^{-1}$) and the trifluoromethyl deformation frequency (736 cm.$^{-1}$), whereas in the compounds $(CF_3)_2PX$ (X = Cl, I) only one band is present. The additional maximum in the case of the aminophosphine could possibly be due to phosphorus–nitrogen stretching, moved to a higher frequency on account of partial double bonding, but on the other hand P–NH_2 vibration is also likely to have an absorption band in this region.

Experimental

Since it was undesirable for the compounds to come into contact with moisture or oxygen, extensive use was made of high-vacuum technique and where this was inconvenient the materials were handled in a nitrogen-filled dry-box containing phosphoric oxide. B. p.s were determined from the vapour-pressure data, and m. p.s were found by using a modification of the Stock type of plunger apparatus. The molecular weights of volatile liquids were

[12] Corbridge, *J. Appl. Chem.*, 1956, **6**, 456.

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determined by Regnault's method. Carbon, hydrogen, and nitrogen percentages were obtained by microcombustion and trifluoromethyl groups as fluoroform liberated on hydrolysis by dilute sodium hydroxide solution.

Materials.—Good commercial chemicals used were purified and dried. The halogenotrifluoromethylphosphines were prepared by the method of Bennett, Emeléus, and Haszeldine,[1] and standard methods were used for the preparation of the other chemicals.

Reactions of Chlorobistrifluoromethylphosphine with Ammonia and Amines.—With the exception of the reaction of aniline, these were carried out in the vapour phase in a cylindrical glass vessel (capacity *ca.* 700 ml.) which had a cold-finger appendage at each end and a manometer for following pressure changes, and was connected with a general-purpose vacuum-system. The halogenotrifluoromethylphosphine was condensed in one of the cold fingers and the amine in the other, and these traps were then allowed to warm to temperatures at which the respective vapour pressures were equal (usually *ca.* 10 mm.). When the reaction was complete the volatile products were removed to the vacuum-system and fractionated before identification. The solid products were removed mechanically after breaking the reaction vessel. The reaction between aniline and chlorobistrifluoromethylphosphine was carried out in the liquid phase in a sealed tube.

(a) *Reaction with ammonia.* Chlorobistrifluoromethylphosphine (8·93 mmoles) and ammonia (17·86 mmoles) at 5 mm. gave ammonium chloride and a volatile liquid which, after fractional condensation to remove traces of the reactants, gave tensimetrically pure *aminobistrifluoromethylphosphine* (1·59 g., 96%) [Found: C, 14·1; H, 1·7; N, 7·7; CF_3, 71·9 (as fluoroform); NH_2, 8·65% (as ammonia); *M*, 186·1. $C_2F_6H_2NP$ requires C, 13·0; H, 1·1; N, 7·58; CF_3, 73·6; NH_2, 8·65%; *M*, 185·0].

(b) *Reaction with methylamine.* Chlorobistrifluoromethylphosphine (6·12 mmoles) and methylamine (12·24 mmoles) at 10 mm. in the vapour phase gave methylamine hydrochloride and *methylaminobistrifluoromethylphosphine* (1·16 g., 95%) [Found: C, 18·2; H, 1·8; N, 7·1; CF_3, 67·3% (as fluoroform); *M*, 200·5. $C_3F_6H_4NP$ requires C, 18·1; H, 2·0; N, 7·0; CF_3, 69·3%; *M*, 199·1].

(c) *Reaction with dimethylamine.* Chlorobistrifluoromethylphosphine (5·5 mmoles) and dimethylamine (11·0 mmoles) at 10 mm. in the vapour phase gave dimethylamine hydrochloride and *dimethylaminobistrifluoromethylphosphine* (0·82 g., 70%) [Found: C, 22·7; H, 2·6; N, 6·6; CF_3, 61·6% (as fluoroform); *M*, 216·5. $C_4F_6H_6NP$ requires C, 22·6; H, 2·8; N, 6·6; CF_3, 64·8%; *M*, 213·1].

(d) *Reaction with aniline.* Aniline (3·63 mmoles) and chlorobistrifluoromethylphosphine (2·01 mmoles) were condensed into a constricted tube which was sealed and allowed to warm to 0°. A vigorous reaction took place, to form aniline hydrochloride and *phenylaminobistrifluoromethylphosphine* (0·3 g., 65%) [Found: C, 36·6; H, 2·5; N, 5·5; CF_3, 51·5% (as fluoroform). $C_9F_6H_6NP$ requires C, 36·8; H, 2·3; N, 5·4; CF_3, 52·9%]. This compound has a pleasant aromatic odour, unlike that of aniline or the chlorophosphine.

Reaction of Tristrifluoromethylphosphine with Ammonia.—Purified tristrifluoromethylphosphine (5·98 mmoles) and ammonia (5·98 mmoles) were mixed in the vapour phase at 22° and 157 mm. The volume of the mixture was equal to the sum of the volumes of the components and apart from the formation of a small trace of white solid (probably ammonium iodide formed by ammonia reacting with a trace of iodophosphines still present in the tristrifluoromethylphosphine) no apparent change occurred. However, liquefying the vapours (−70°) for 30 min. and re-warming the mixture to room temperature afforded a less volatile liquid and the pressure had decreased. Repetition of this procedure resulted in an increase in the amount of the less volatile liquid. The volatile contents of the reaction vessel were fractionally condensed several times and in addition to ammonia and tristrifluoromethylphosphine the following were separated: fluoroform (1·72 mmoles) (Found: *M*, 69·0. Calc. for CHF_3: *M*, 70·0), aminobistrifluoromethylphosphine (0·54 mmole) (Found: *M*, 173. The infrared spectrum of this material indicated that it contained a trace of ammonia), and an involatile liquid of unknown structure.

Reaction between Iodobistrifluoromethylphosphine and Sodamide.—Iodobistrifluoromethylphosphine (1·42 mmoles) and sodamide (2·7 mmoles) were sealed together in a tube and set aside for 24 hr. at room temperature. Examination of the vapour in the tube showed it to be unchanged iodobistrifluoromethylphosphine (1·34 mmoles, 94·5%) (Found: *M*, 292·5. Calc. for C_2F_6IP: *M*, 296·0).

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Reaction of Iodobistrifluoromethylphosphine with Phosphine.—Iodobistrifluoromethylphosphine (3·49 mmoles) was mixed with phosphine (6·98 mmoles) in the vapour phase. In 12 hr. at 20° the pressure fell from 276 mm. to 187 mm., and the wall of the reaction vessel was coated with a reddish-brown deposit (phosphorus) and some large white transparent crystals (phosphonium iodide). Repeated fractional distillation of the volatile contents of the vessel gave unchanged phosphine (0·145 g., 61·4%) (Found: *M*, 34·5. Calc. for PH_3: *M*, 34·0), iodobistrifluoromethylphosphine (0·07 g., 6·8%) (Found: *M*, 285·5), and bistrifluoromethylphosphine (0·43 g., 73%) (Found: C, 13·9; H, 0·7%; *M*, 168·5. Calc. for C_2F_6HP: C, 14·1; H, 0·59%; *M*, 170). The identity of this material was confirmed by its infrared spectrum. During the separation of these compounds by fractional condensation an orange-red solid was deposited in the traps and this probably consists mainly of phosphorus di-iodide (Found: I, 87·3. Calc. for P_2I_4: I, 89·1%) formed when phosphine and iodobistrifluoromethylphosphine are present together in the liquid state during the distillation.

Treatment of Chlorobistrifluoromethylphosphine with Hydrogen Sulphide.—Hydrogen sulphide (2·95 mmoles) and chlorobistrifluoromethylphosphine (2·95 mmoles) did not react when mixed in the vapour phase at 20° for 12 hr., or in the liquid phase at −76° for several hours. The mixture was fractionated, giving unchanged hydrogen sulphide (0·096 g., 95%) (Found: *M*, 37·9. Calc. for H_2S: *M*, 34·1), and chlorobistrifluoromethylphosphine (0·575 g., 95·3%) (Found: *M*, 205. Calc. for C_2ClF_6P: *M*, 204·5) of known infrared spectrum.

Properties of the Aminobistrifluoromethylphosphines.—The aminobistrifluoromethylphosphines are colourless liquids (see Table). They appear to be readily oxidised by air (aminobistrifluoromethylphosphine is spontaneously inflammable), but can be kept unchanged indefinitely (as is indicated by the constancy of vapour pressures and molecular weights) in a sealed Pyrex tube at 0°. There is no reaction with mercury.

Vapour-pressure determination. Except in the case of the involatile phenylaminobistrifluoromethylphosphine, vapour pressures were determined from room temperature down to a temperature at which the vapour pressure of the liquid was *ca.* 1 mm. Pressures were obtained from a wide-bore mercury manometer in a system which incorporated a Pyrex-glass spiral-gauge null-meter. The thermostat bath consisted of a Dewar flask containing a suitable stirred liquid (usually acetone); cooling was achieved by adding small pieces of solid carbon dioxide and the bath was warmed by the addition of suitable quantities of the liquid. Fairly efficient temperature-control was obtained by this procedure and vapour pressures at ascending and descending temperatures were coincident. A pentane thermometer was used for low-temperature measurement. The vapour pressure of phenylaminobistrifluoromethylphosphine was measured in the range 24—145° by means of a mercury isoteniscope.

Action of Heat on Aminobistrifluoromethylphosphine.—Known weights of aminobistrifluoromethylphosphine were heated in sealed Carius tubes at 78°, 180°, 218°, 250°, 300°, and 370° severally for 48 hr. From the tubes heated to $\geqslant$250° the compound was recovered almost quantitatively (>90%). After 48 hr. at 300° only 75% of the aminophosphine was recovered, and among the volatile decomposition products (identified by their infrared spectra) were fluoroform, phosphorus fluorides, and silicon tetrafluoride (presumably from attack on the glass by hydrogen fluoride). At 370° aminobistrifluoromethylphosphine was decomposed completely and there was a deposit of carbon. The volatile products contained nitrogen which was removed at a Töpler pump, and the condensable material was resolved into a very volatile and a less volatile portion by fractional condensation. By means of their infrared spectra the former was shown to consist of a mixture of fluoroform, phosphorus fluorides and silicon tetrafluoride, and the latter identified as hydrogen cyanide (Found: *M*, 28·6. Calc. for HCN: *M*, 27·0).

Hydrolysis of Aminobistrifluoromethylphosphines.—(1) *Aminobistrifluoromethylphosphine.* (*a*) Water. The aminophosphine (7·39 mmoles) was sealed in a Carius tube with distilled water (7 ml.) and left for 48 hr. at 20°. The volatile products were fractionated, yielding fluoroform (7·41 mmoles) (Found: *M*, 70·4). The aqueous hydrolysate reduced warm mercuric chloride solution. Freeze-drying of the solution recovered from the Carius tube gave a very hygroscopic white solid which, from its infrared spectrum, appeared to be ammonium trifluoromethylphosphonite, $CF_3{\cdot}PHO{\cdot}ONH_4$, and not the possible alternative, trifluoromethylphosphonamidous acid, $CF_3{\cdot}P(NH_2){\cdot}OH$.

(*b*) Acid. Aminobistrifluoromethylphosphine (9·76 mmoles) and N-hydrochloric acid (10 ml.) were sealed in a Carius tube and kept for 14 days at 20°. Fractionation of the volatile products

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gave fluoroform (9·67 mmoles) (Found: *M*, 69·9). The ammonium ion content of the hydrolysate was estimated by semi-micro Kjeldahl analysis: [13] the total amount of ammonia liberated was 9·74 mmoles. The solution left in the Carius tube reduced warm aqueous mercuric chloride. After oxidation of this solution by boiling (30%) aqueous hydrogen peroxide, neutralisation with dilute potassium hydroxide solution, then freeze-drying, gave a white solid whose infrared spectrum indicated the presence of potassium trifluoromethylphosphonate, $CF_3 \cdot PO(OK)_2$.

(*c*) Alkali. The aminophosphine (1·134 mmoles) and 10% sodium hydroxide solution (10 ml.) were sealed in a Carius tube and left at 20° for 14 days. The volatile products were shaken with N-hydrochloric acid (25 ml.) to dissolve liberated ammonia. The remainder of the volatile hydrolysis product was fractionated and shown to be fluoroform (2·19 mmoles) (Found: *M*, 69·4). The ammonia produced by hydrolysis was estimated as before (1·067 mmoles). A portion of the original hydrolysate was freeze-dried and sodium phosphite was identified in the solid residue by means of its infrared spectrum.

(2) *Methylaminobistrifluoromethylphosphine.* (*a*) Water. The aminophosphine (0·538 mmole) was distilled into a hydrolysis bulb containing distilled water (8 ml.) and the reaction allowed to proceed for 48 hr. at 20°. The bulb was then opened to the vacuum-system and fractionation of the volatile products yielded fluoroform (0·468 mmole) (Found: *M*, 69·5).

(*b*) Alkali. Methylaminobistrifluoromethylphosphine (0·913 mmole), sealed in a Carius tube with 10% sodium hydroxide solution (8 ml.) and left for 24 hr. at room temperature, gave volatile materials which were distilled into a bulb containing N-hydrochloric acid (25 ml.). This was shaken to absorb any amine (NH_2Me) present in the vapour phase, and then the remaining volatile materials was fractionated. This yielded fluoroform (1·88 mmole) (Found: *M*, 69·6). The solution left in the Carius tube reduced mercuric chloride in the cold.

(3) *Dimethylaminobistrifluoromethylphosphine.* (*a*) Water. Dimethylaminobistrifluoromethylphosphine (0·826 mmole) and distilled water (8 ml.) were sealed in a hydrolysis bulb and left at room temperature, but the aminophosphine did not dissolve completely. However, partial hydrolysis had occurred since fractionation of the volatile materials yielded fluoroform (0·123 mmole) (Found: *M*, 70·0).

(*b*) Alkali. The aminophosphine (0·982 mmole) and 10% sodium hydroxide solution (7 ml.) were sealed in a Carius tube: at room temperature two liquid phases were present. Hence the tube was heated at 88—94° for 48 hr. at the end of which no insoluble material remained. The volatile products were shaken in a bulb containing N-hydrochloric acid to remove amine and/or ammonia vapour, then fractionated, yielding fluoroform (1·866 mmoles) (Found: *M*, 70·2). The aqueous hydrolysate contained a component which reduced mercuric chloride.

(4) *Phenylaminobistrifluoromethylphosphine.* (*a*) Water. The aminophosphine (0·128 mmole) and distilled water (3 ml.) were allowed to react in a sealed tube at room temperature for 2 weeks. The compound dissolved in the water and the volatile product of hydrolysis was fluoroform (0·134 mmole) (Found: *M*, 74·0), isolated after fractionation. The solution left in the tube was acidic and reduced mercuric chloride on warming.

(*b*) Alkali. Phenylaminobistrifluoromethylphosphine (0·423 mmole) was hydrolysed by 10% sodium hydroxide solution (5 ml.) in a sealed Carius tube heated to 120° for 48 hr. At the end of this period the alkali contained oily globules (aniline), and fluoroform (0·823 mmole) (Found: *M*, 70·5) was obtained as the only volatile product of hydrolysis. The solution left in the tube had an odour of aniline and reduced mercuric chloride in the cold.

Reaction of Aminobistrifluoromethylphosphine with Hydrogen Chloride.—Aminobistrifluoromethylphosphine (0·62 mmole) and excess of hydrogen chloride were sealed together in a tube, and at −64° a vigorous reaction occurred, one product of which was ammonium chloride. The volatile contents of the tube were fractionated and, after removal of the excess of hydrogen chloride, chlorobistrifluoromethylphosphine (0·52 mmole) (Found: *M*, 200) was obtained.

Reaction of Aminobistrifluoromethylphosphine with Chlorine.—Chlorine (10·3 mmoles) and aminobistrifluoromethylphosphine (2·0 mmoles) were allowed to interact in a sealed tube at −78° but no reaction appeared to occur at this temperature and the tube was allowed slowly to warm to 20°. During this, effervescence occurred and a white solid was produced. This was identified as ammonium chloride by its infrared spectrum. The liquid was fractionated

[13] Belcher and Godbert, "Semi-micro Quantitative Organic Analysis," Longmans, Green & Co., London, 1954, p. 89.

several times and split into a very volatile fraction, a middle fraction which was mainly chlorine, and a fraction of low volatility. The very volatile fraction was sealed in a tube containing 10% sodium hydroxide solution, shaken for some time, and fractionated, giving only a small amount of very volatile material which, from its infrared spectrum, appeared to be chlorotrifluoromethane. The involatile fraction had an estimated molecular weight of 236 and chlorine analysis gave 24·6% (by precipitation as silver chloride after hydrolysis). The material gave ammonia when boiled with dilute alkali. A white solid (presumably ammonium chloride) was slowly formed in the liquid. From this evidence it is not possible to assign a structure to this substance, but it is probably a mixture of bistrifluoromethylphosphorus trichloride, $(CF_3)_2PCl_3$ (which is formed when chlorobistrifluoromethylphosphine reacts with chlorine), and an addition compound of chlorine and aminobistrifluoromethylphosphine, $[(CF_3)_2P{\cdot}NH_2,Cl_2]$, which slowly decomposes at room temperature.

Attempted Preparation of a Salt of Aminobistrifluoromethyl Phosphine.—(a) *Silver salt.* Equimolar quantities (0·69 mmole) of silver nitrate and aminobistrifluoromethylphosphine were dissolved in pyridine (1·2 ml.). The solution, originally colourless, became yellow and then orange-brown; no solid could be crystallised and removal of the solvent under vacuum left an involatile viscid liquid whose infrared spectrum indicated the presence of pyridine as well as a $(CF_3)_2P$-component.

(b) *Sodium salt.* Aminobistrifluoromethylphosphine (1·75 mmoles) and sodamide (1·38 mmoles) were allowed to react in a sealed tube at room temperature. Effervescence occurred and in place of the mobile aminophosphine, a gelatinous substance was formed. The volatile products were fractionated, yielding fluoroform (0·69 mmole) (Found: *M*, 69·1) and unchanged aminobistrifluoromethylphosphine (0·33 mmole) (identified by its infrared spectrum) together with a trace of ammonia. The residue is presumably some kind of phosphorus–nitrogen polymer; its infrared spectrum suggests the presence of trifluoromethyl groups.

Conductance Measurements.—These were made with a small cell (capacity *ca.* 1·5 ml.) with smooth platinum electrodes (cell constant, 0·8233 cm.$^{-1}$). Solutions were prepared by weight and introduced into the cell by distillation in the vacuum-system. Resistances were measured at 25° by the Wheatstone bridge circuit described by Haszeldine and Woolf.[14]

Infrared Spectra.—The spectra were measured on a Perkin-Elmer Model 21 Spectrometer with rock-salt optics. The compounds were studied in the vapour state (in a 100 mm. cell) with the exception of phenylaminobistrifluoromethylphosphine, which was examined as a liquid film. In the following list the figures are in cm.$^{-1}$ and the letters have their usual meaning.

$(CF_3)_2P{\cdot}NH_2$: 3490s, 3380s, 3100w, 2520w, 2360w, 2260m, 1954w, 1898w, 1856w, 1760w, 1675w, 1569s, 1366m, 1282s, 1207s, 1160s, 1115s, 976s, 888s, 736s, 675m.

$(CF_3)_2P{\cdot}NHMe$: 3400m, 3430s, 2930s, 2830m, 2260m, 1897w, 1675w, 1566w, 1487m, 1464m, 1440m, 1394s, 1280m, 1206s, 1157s, 1112s, 998w, 807s, 732m.

$(CF_3)_2P{\cdot}NMe_2$: 3030w, 2980s, 2910s, 2870s, 2810s, 2380w, 2300m, 2250m, 1990w, 1890w, 1687m, 1625w, 1487s, 1467s, 1385m, 1298s, 1200s, 1155s, 1112s, 1069s, 1000s, 880w, 805w, 742m, 690s.

$(CF_3)_2P{\cdot}NHPh$: 3375m, 3350m, 3045m, 2260w, 1940w, 1845w, 1705w, 1605s, 1503s, 1477m, 1390m, 1380m, 1335w, 1282s, 1238s, 1200s, 1148s, 1103s, 1032m, 1000w, 920s, 793m, 748s, 688s.

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[14] Haszeldine and Woolf, *Chem. and Ind.*, 1950, 544.

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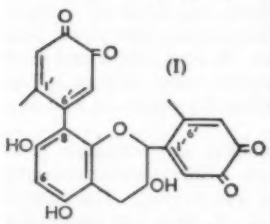
91. *Autoxidation of Polyphenols. Part IV.* Oxidative Degradation of the Catechin-autoxidation Polymer.*

By D. E. Hathway.

It has now been found that permanganate oxidation of the methylated hydrogenation product of catechin-autoxidation polymer (Part III) gives *m*-hemipinic, veratric, and oxalic acid, whereas similar oxidation of the methylation product of the polymer produced by acid catalysis [1] yields veratric and oxalic acid. The difficulty involved in the oxidative degradation of aromatic polymers is shown by the low yield (9%) of veratric acid from the acid-catalysis polymer which is a dimer or trimer.[1] Secondary oxidation which occurs during the preparation of the autoxidation polymer (Part III) is paralleled by a 70% uptake of hydrogen during hydrogenation of the polymer. Its behaviour on dialysis through cellophane indicates that this polymer is a higher polymer than that given by acids, and the more difficult degradation led to a smaller proportion of aromatic acids. *m*-Hemipinic acid (2%) is accompanied by 0·5% of veratric acid, the latter arising presumably from end-groups. These experiments suggest that autoxidation of catechin leads to some polymerisation by type (I) linkages, whereas acids lead to some union of the Freudenberg type.



Catechin-autoxidation polymer is important on account of its close structural similarity to phlobatannins, which have recently been isolated in high yield from the extractives of harvested *Uncaria gambir* leaves and *Acacia catechu* heartwood.[2]

Experimental.—M. p.s were determined on a Kofler block. Paper chromatography was carried out in all-glass apparatus in a constant-temperature enclosure at 25°. Chromatograms were dried in a current of warm air at 60°. Tubes (1·8 cm. in diameter) fitted with a tap of 4 mm. bore and a sintered-glass disc were packed with "chromatographic" silica gel (20 g.) (from Messrs. L. Light & Co.), which had been mixed with 0·5N-sulphuric acid (10 ml.) and made into a slurry with chloroform (60—70 ml.), by Bulen, Varner, and Burrell's method.[3] Eluants were prepared by the equilibration of appropriate volumes of butan-1-ol and chloroform with a little water, and retention of the lower phase.

m-Hemipinic acid (m. p. 179—182°) was prepared from *m*-meconine [4] (Found: C, 53·5; H, 4·8%; equiv., 115. Calc. for $C_{10}H_{10}O_6$: C, 53·1; H, 4·5%; equiv., 113).

Chromatographic separation of veratric and m-*hemipinic acid.* Marker spots (5 μl.) of 0·5% w/v chloroform solutions of the acids were applied to start-lines, 4 cm. from the lower edge of Whatman filter paper No. 1, of length 57 cm. Single-way ascending chromatography was effected with the systems: (1) benzyl alcohol–*tert.*-butyl alcohol–*iso*propyl alcohol–water (3 : 1 : 1 : 1, by vol.) containing 1·8% w/v of formic acid; [5] (2) propanol–35% aqueous ammonia–water (6 : 3 : 1, by vol.).[6] Papers were irrigated for 20 hr. When the chromatograms were developed with solvent system (1), the acids were exposed as yellow spots against a green background by means of a solution of bromocresol-green at pH 5·5; [7] when they were developed with system (2), the acids were revealed by Universal indicator (British Drug Houses Ltd.), adjusted to pH 9—10,[8] as red spots which faded fairly rapidly. *m*-Hemipinic acid had R_F 0·78 (1), 0·53 (2), and veratric acid had R_F 0·95 (1), 0·76 (2).

* Part III, *J.*, 1957, 1562.

[1] Freudenberg and Maitland, *Annalen*, 1934, **510**, 193; *Collegium*, 1934, **776**, 656; Freudenberg, Stocker, and Porter, *Chem. Ber.*, 1957, **90**, 957.
[2] Hathway and Seakins, *Biochem. J.*, 1957, **65**, 32P; **67**, 239.
[3] Bulen, Varner, and Burrell, *Analyt. Chem.*, 1952, **23**, 187.
[4] Edwards, Perkin, and Stoyle, *J.*, 1925, **127**, 195.
[5] Stark, Goodban, and Owens, *Analyt. Chem.*, 1952, **23**, 413.
[6] Hanes and Isherwood, *Nature*, 1949, **164**, 1107.
[7] Lugg and Overell, *ibid.*, 1947, **160**, 87.
[8] Long, Quayle, and Stedman, *J.*, 1951, 2197.

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A solution of veratric (50 mg.) and *m*-hemipinic (50 mg.) acid in methanol–chloroform (1 : 1 by vol.; 1 ml.) was added to the top of the column and allowed to drain into the column. The column was eluted successively with chloroform (50 ml.) and 1 : 40 v/v butan-1-ol–chloroform (100 ml.) at a flow-rate of 2 ml./min., solvent being added in 50 ml. volumes before the last 10 ml. of the preceding volume had drained into the column. The effluent was collected in 10 ml. fractions, in which the acid was estimated after the addition of water by titration with 0·01N-sodium hydroxide. Separation was very efficient.

Permanganate oxidation of the methylated hydrogenation product of catechin-autoxidation polymer. A methanolic solution (130 ml.) of catechin-autoxidation polymer (700 mg.) (Part III) was hydrogenated at 1 atm., in the presence of Adams catalyst, and then treated with diazomethane. The product (700 mg.) in dioxan (25 ml.) and saturated aqueous sodium carbonate (2·5 ml.) at 100° was gradually treated with N-potassium permanganate (70 ml.). After the reduction, the filtrate was concentrated to 25 ml., and acidified with 12N-hydrochloric acid. The resinous precipitate (360 mg.) was removed, and the filtrate neutralised to Congo-red with sodium acetate and treated with excess of 0·5M-calcium chloride. The supernatant liquid was centrifuged off, and the calcium oxalate (280 mg.) washed and dried at 100°. Ether-extraction of the combined supernatant liquid and washings, after saturation with sodium chloride and acidification with 12N-hydrochloric acid, afforded a partly crystalline ochreous residue (120 mg.) which on partition chromatography on silica gel gave a sharp fraction (10 mg.) which was recovered by chloroform extraction of the re-acidified fractions. Crystallisation from xylene–light petroleum (b. p. 100—120°) gave *m*-hemipinic acid (9 mg.), m. p. and mixed m. p. 179—182° (anhydride sublimed at 175°). A second fraction (10 mg.), crystallised from xylene–light petroleum, gave veratric acid, m. p. and mixed m. p. 179—180°.

Permanganate oxidation of the methylation product of acid-catalysis polymer. A solution of the methylated polymer [1] (3 g.) in dioxan (100 ml.) and saturated aqueous sodium carbonate (10 ml.) at 100° was similarly treated with aqueous N-potassium permanganate (350 ml.). The filtrate was concentrated to 100 ml. and acidified with 12N-hydrochloric acid, and the precipitate (1·5 g.) obtained was extracted with boiling water (500 ml.) (charcoal). Evaporation of the filtrate to 20 ml. gave a precipitate (200 mg.), m. p. 165—180°, which was removed in the centrifuge, and dried (KOH) at 20°/0·05 mm. When a 30 mg. portion was submitted to partition chromatography on silica gel, a sharp fraction (26 mg.) was eluted which, crystallised from xylene–light petroleum (b. p. 100—120°), gave needles of veratric acid, m. p. and mixed m. p. 179—180°. Absence of *m*-hemipinic acid was shown by paper chromatography.

Calcium oxalate (950 mg.) was separated from the initial filtrate.

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British Leather Manufacturers' Research Association,
Milton Park, Egham, Surrey. [*Received, July 25th*, 1957.]

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92. *Compounds of Silicon. Part III.* Competitive Reactions of Chloro-, Bromo-, and Iodo-triethylsilanes with Phenol.*

By R. A. Shaw.

Recent work by Wilkins and his co-workers [1,2,3] prompts publication of some results obtained by us several years ago. A theory of the relative ease of displacement of the halogen in trialkylhalogenosilanes has been proposed for reactions proceeding by a simple bimolecular mechanism,[2] $Y^- + R_3SiX \longrightarrow R_3SiY + X^-$. It was suggested that, providing steric effects are here not significant, the relative ease of displacement of the group X

* Part II, *J.*, 1957, 2831.

[1] Wilkins, Brown, and Stevens, *J.*, 1950, 163.
[2] Vaughan and Wilkins, *Nature*, 1951, **167**, 525.
[3] Reid and Wilkins, *J.*, 1955, 4029.

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in a competitive reaction, where the same reagent Y^- competes for different halogenosilanes R_3SiX and R_3SiX', depends on the respective values of the electron affinities of the halogen atoms E_X less the bond energies of the silicon–halogen bonds B_{Si-X}, *i.e.* $E_X - B_{Si-X}$, which represents the " ionic bond energy " [4] less a constant (the ionisation potential of silicon). The " ionic bond energies " of the silicon–halogen bonds, which have been discussed,[4,5] and recently revised [5] in the light of the more accurate data now available, are Si–I 167·4, Si–Br 179·0, Si–Cl 190·3, and Si–F 237·4 (kcals. mole^{-1}).

Competitive reactions of chloro-, bromo-, and iodo-triethylsilanes with phenol in carbon tetrachloride solution confirm this order qualitatively. The reactivity ratio for this reaction of Si–I/Si–Br was found to be 15—20 : 1, and that of Si–Br/Si–Cl 3—4 : 1. From this one would expect a value of 45—80 : 1 for the Si–I/Si–Cl ratio, and the experimental values lay in the region of 45—70 : 1. As neither of the silanes was present in large excess, the concentration of the more reactive halides decreased rapidly in the course of the reaction, and the above ratios are lower limiting values of the true ones. A further effect which also tended to diminish the reactivity ratios was the reversibility of the reaction $Et_3SiX + PhOH \rightleftharpoons Et_3Si{\cdot}OPh + HX$, which was at least partially overcome by aspirating a stream of dry nitrogen through the mixture.

Experimental.—Preparation of reagents. Chloro-,[6] b. p. 145—146°, bromo-,[6] b. p. 162—163°, and iodo-triethylsilane,[7] b. p. 188—188·5°, were prepared by Eaborn's methods.[6,7] Carbon tetrachloride was dried (P_2O_5) and distilled. All these reagents were fractionally distilled in a column of approximately ten theoretical plates. " AnalaR " phenol was distilled and the centre cut collected.

Competitive reactions of halogenosilanes with phenol. Accurately weighed amounts of the two halogenosilanes and phenol (slightly less than the quantity corresponding to the smaller of the two silane concentrations) were dissolved in carbon tetrachloride (10 ml.) and a fast stream of dry nitrogen passed through the solution. The iodine : bromine and the iodine : chlorine ratios were determined at room temperature, the bromine : chlorine ratio at the b. p. of the solvent. The hydrogen halides evolved were absorbed in sodium hydroxide solution; a control flask containing aqueous silver nitrate showed that all of the hydrogen halide was absorbed.

Estimation of the mixed halide ions. The mixed halide ions were determined by potentiometric titration, a quinhydrone electrode, a salt bridge, and a silver electrode being used. Known volumes of the absorbing alkaline solutions were withdrawn from time to time and made up to known volumes, aliquot parts of which were titrated with 0·1N-silver nitrate after acidification with dilute nitric acid. The titrations were followed by means of a Mullard " magic eye " indicator. The accuracy of the method was checked by using standard solutions of mixed halide ions. The reactivity ratios are the results of several runs and of different stages of completion of the reaction. A typical runs was as follows: Bromotriethylsilane (2·804 g., 0·01435 mole), iodotriethylsilane (1·220 g., 0·00505 mole), and phenol (0·440 g., 0·00468 mole) were used in carbon tetrachloride (10 ml.). After ½ hr. (50% reaction) the mean of three titres gave the reactivity ratio (corrected for the different concentrations of the halogenosilanes) as 20 : 1; after 1½ hr. (83% reaction) 15·5 : 1. If the stream of nitrogen was fast enough, the ratio reached a limiting value; slower rates of gas passage decreased this value, owing to the reversible reaction discussed above.

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BIRKBECK COLLEGE, MALET STREET, LONDON, W.C.1. [*Received, June 19th,* 1957.]

[4] Eaborn, *J.*, 1950, 3077.
[5] Shaw, *J.*, 1957, 2831.
[6] Eaborn, *J.*, 1953, 494.
[7] *Idem*, *J.*, 1949, 2755.

93. *Direct 5-Hydroxylation of 3β-Acetoxyandrostane-11 : 17-dione.*

By M. Martin-Smith.

During the work directed towards a partial synthesis of aldosterone,[1] a secondary product was always obtained in small yield in the preparation of 3β-acetoxyandrostane-11 : 17-dione from 3β-acetoxy-17α-hydroxy*allo*pregnane-11 : 20-dione by the action of chromic oxide in aqueous aceti cacid. This compound has now been characterized as 3β-acetoxy-5α-hydroxyandrostane-11 : 17-dione and its direct formation from 3β-acetoxyandrostane-11 : 17-dione demonstrated. Its constitution, which was conclusively shown by its conversion in several steps into adrenosterone, was made apparent from its infrared spectrum, from molecular-rotational considerations,[2] and by analogy with the earlier direct 5-hydroxylation of steroids reported by St. André *et al.*[3]

Extensive investigation of reaction conditions failed to raise the yield of 3β-acetoxy-5α-hydroxyandrostane-11 : 17-dione from 3β-acetoxyandrostane-11 : 17-dione above 14%. It therefore appears not to be feasible to use direct 5-hydroxylation by this method as a means of obtaining 3β : 5α-dihydroxy-steroids for conversion into the 3-keto-Δ^4-compounds which constitute many biologically important steroids (cf. Bladon *et al.*[4]).

In accordance with expectations 3β-acetoxy-5α-hydroxyandrostane-11 : 17-dione was readily dehydrated to 3β-acetoxyandrost-5-ene-11 : 17-dione. Also boiling methanolic sodium hydroxide solution deacetylated 3β-acetoxy-5α-hydroxyandrostane-11 : 17-dione to the corresponding dihydroxy-dione. Oxidation of this compound by chromic oxide in pyridine yielded 5α-hydroxyandrostane-3 : 11 : 17-trione which thionyl chloride in ice-cold pyridine dehydrated smoothly to androst-4-ene-3 : 11 : 17-trione (adrenosterone).

Experimental.—$[\alpha]_D$ are in $CHCl_3$; ultraviolet absorption spectra refer to EtOH solutions; infrared spectra were taken in Nujol suspension. M. p.s were taken on a Kofler block.

3β-Acetoxy-5α-hydroxyandrostane-11 : 17-dione. Maximum yields were to be obtained by the following procedure. A solution of chromic oxide (4·0 g.) in water (3 ml.) was diluted to 100 ml. by glacial acetic acid. 3β-Acetoxyandrostane-11 : 17-dione (500 mg.) was treated with this solution (10 ml.), and the mixture kept at room temperature for 26 hr. Methanol in excess was added and after 3 hr. at room temperature the solution was taken to dryness under reduced pressure. The residue was treated with dilute hydrochloric acid and extracted with chloroform (5 × 20 ml.). The chloroform extracts were washed with sodium hydrogen carbonate solution and water, and taken to dryness under reduced pressure, yielding a colourless oil. This was chromatographed in benzene over alumina (Brockmann grade V). Benzene eluted unchanged starting material. Benzene–chloroform (4 : 1) eluted deacetylated starting material. Chloroform eluted the 5α-hydroxy-compound. Reacetylation of the deacetylated starting material (identical with 3β-hydroxyandrostane-11 : 17-dione [5]) by overnight treatment with acetic anhydride in pyridine afforded a total recovery of 3β-acetoxyandrostane-11 : 17-dione of 60%.

Crystallisation from methanol gave the *3β-acetoxy-5α-hydroxyandrostane-11 : 17-dione* as blunt prisms (70 mg., 14%), showing change of crystal form *ca.* 190° and melting at 244·5—246·5°, $[\alpha]_D$ +86° (*c* 2·08) (Found: C, 69·9; H, 8·7. $C_{21}H_{30}O_5$ requires C, 69·6; H, 8·4%). Longer reaction times did not increase the yield of the 5α-hydroxy-compound, but led to lower recoveries of starting material.

3β-Acetoxy-5α-hydroxyandrostane-11 : 17-dione is soluble in benzene, chloroform, methanol, and ethanol, sparingly soluble in ether, and insoluble in water. The ultraviolet spectrum showed a plateau at *ca.* 290 mμ, ε ~100 (isolated keto-groups) but no other absorption. The infrared spectrum showed a peak at 3480 (OH), a broad peak at 1728—1720 (acetate and 5-membered cyclic ketone), and peaks at 1700 (6-membered cyclic ketone) and 1244 cm.$^{-1}$ (acetate).

[1] Barton, Campos-Neves, and Scott, *J.*, 1957, 2698.
[2] Barton and Klyne, *Chem. and Ind.*, 1948, 755; Fieser and Fieser, "Natural Products Related to Phenanthrene," Reinhold Publ. Corp., New York, 3rd edn., 1949, pp. 204—219.
[3] St. André, MacPhillamy, Nelson, Shabica, and Scholz, *J. Amer. Chem. Soc.*, 1952, **74**, 5506.
[4] Bladon, Henbest, Jones, Lovell, and Woods, *J.*, 1954, 125.
[5] Klyne and Ridley, *J.*, 1956, 4825; Steiger and Reichstein, *Helv. Chim. Acta*, 1937, **20**, 817.

XUM

3β-*Acetoxyandrost*-5-*ene*-11 : 17-*dione*. 3β-Acetoxy-5α-hydroxyandrostane-11 : 17-dione (140 mg.) in ice-cold pyridine (5 ml.) was treated with ice-cold thionyl chloride (0·2 ml.) and kept at 0° for 10 min. The mixture was then poured into water (50 ml.): the crystalline unsaturated *dione* was deposited. It was collected, dried at the pump, and extracted with warm methanol (20 ml.). Concentration of the solution afforded plates, m. p. 166—167°. Further crystallization from ethyl acetate–light petroleum (b. p. 40—60°) yielded plates, m. p. 170—171·5° (70 mg.) (Found: C, 72·9; H, 8·2. $C_{21}H_{28}O_4$ requires C, 73·2; H, 8·2%). The ultraviolet spectrum showed end-absorption and a weak maximum near 290 mμ, $[\alpha]_D$ +38° (*c* 2·11). The infrared spectrum showed a broad peak at 1740—1727 (acetate and 5-membered cyclic ketone) and peaks at 1707 (6-membered cyclic ketone), 1663 (isolated double bond), 1248 (acetate), and 812 cm.$^{-1}$ (trisubstituted double bond). Hydrogenation in acetic acid solution in the presence of Adams catalyst afforded 3β-acetoxyandrostane-11 : 17-dione (identity proved by infrared spectrum in KCl disc).

3β : 5α-*Dihydroxyandrostane*-11 : 17-*dione*. 3β-Acetoxy-5α-hydroxyandrostane-11 : 17-dione (100 mg.) was refluxed for 1 hr. with sodium hydroxide (500 mg.) in methanol (10 ml.). The mixture, on being poured into water (75 ml.), deposited a colourless solid (65 mg.). A further 20 mg. of material was obtained by chloroform-extraction of the aqueous solution. Crystallized from methanol, the product formed stout rods which changed to needles at 250° and melted at 273—274° (Found: C, 71·1; H, 8·4. $C_{19}H_{28}O_4$ requires C, 71·2; H, 8·8%). This *dione* is sparingly soluble in ether and only moderately soluble in chloroform and dioxan. $[\alpha]_D$ was therefore taken in pyridine [+137° (*c* 1·96)]. The infrared spectrum showed peaks at 3430, 3350 (OH), 1727 (5-membered cyclic ketone), and 1700 cm.$^{-1}$ (6-membered cyclic ketone).

5α-*Hydroxyandrostane*-3 : 11 : 17-*trione*. Pyridine–chromic oxide complex was prepared by adding finely ground chromic oxide (100 mg.) in small portions to pyridine (1 ml.) with cooling. To the resulting slurry was added 3β : 5α-dihydroxyandrostane-11 : 17-dione (80 mg.), dissolved in pyridine (2 ml.). The mixture, which became homogeneous, was kept overnight at room temperature, then diluted to 100 ml. with water and acidified with dilute hydrochloric acid. Extraction with chloroform (3 × 25 ml.) gave a dark red extract which, on being extracted with dilute aqueous sodium hydroxide solution followed by water, lost nearly all its colour. The chloroform solution was taken to dryness under reduced pressure and the resulting brown amorphous residue exhaustively extracted with ether. The ethereal extracts yielded a white solid which on crystallization from ethanol formed prisms, m. p. 241—243° (Found: C, 71·8; H, 7·9. $C_{19}H_{26}O_4$ requires C, 71·7; H, 8·2%), of the *trione*. Crystallization of this from methanol–ether gives a cubic form, m. p. 252—254°. Slow heating of the prisms of m. p. 241—243° also converts them into the higher-melting form, $[\alpha]_D$ +145° (*c* 1·50). The infrared spectrum showed peaks at 3490 and 3440 (OH), 1730 (5-membered cyclic ketone), and 1705 and 1690 cm.$^{-1}$ (6-membered cyclic ketone).

Adrenosterone. 5α-Hydroxy-3 : 11 : 17-trione (60 mg.), dissolved in pyridine (2 ml.), was cooled to 0°. Then chilled thionyl chloride (0·1 ml.) was added and the mixture set aside at 0° for 10 min. It was then diluted to 100 ml. with water, acidified with hydrochloric acid, and extracted with ether (3 × 100 ml.). The ethereal extracts were washed with water and taken to dryness under reduced pressure, yielding a colourless solid (40 mg.). Crystallization from ether gave cubes, m. p. 218—220°, $[\alpha]_D$ +286° (*c* 0·95), $\lambda_{max.}$ 238 mμ (ε 1·53 × 10^4) [reported for adrenosterone: m. p. 218—220°,[6] 221—225°,[7] 222—224°,[8] $[\alpha]_D$ +284°,[7] $\lambda_{max.}$ 239 mμ (ε 1·38 × 10^4) [8]].

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THE UNIVERSITY, GLASGOW, W.2. [*Received, August 7th*, 1957.]

[6] Mason and Sprague, *J. Biol. Chem.*, 1948, **175**, 451.
[7] Fried, Thoma, Gerke, Herz, Dorin, and Perlman, *J. Amer. Chem. Soc.*, 1952, **74**, 3962.
[8] Sarett, *J. Biol. Chem.*, 1946, **162**, 601.

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94. *Sulphide Ratio in the Decomposition of Ethyldimethylsulphonium Bromide.*

By Y. Pocker.

Decompositions of trimethylsulphonium hydroxide and phenoxide in ethanol were found by Gleave, Hughes, and Ingold [1] to give second-order kinetics and were interpreted as bimolecular nucleophilic substitutions. Decomposition of the corresponding carbonate, iodide, bromide, and chloride followed first-order kinetics and had the same rate-constant, being interpreted as unimolecular nucleophilic substitutions.

Streitwieser [2] criticised the unimolecular interpretation, arguing that a bimolecular displacement by solvent ethanol would be equally consistent with the results. This is an unacceptable criticism. Gleave, Hughes, and Ingold gave an independent way of arriving at an answer. The decomposition of the trimethylsulphonium bromide and chloride was measured, by following the disappearance of halide ions. Since ethyl methyl ether is relatively stable under the experimental conditions the primary substitution products must be the corresponding methyl halides. On the other hand, each bimolecular act of substitution by ethanol must yield ethyl methyl ether, dimethyl sulphide, and hydrogen *halide*, leading to $d(Halide^-)/dt = 0$, contrary to observations. Since the various methyl halides are formed at the same rate from the corresponding trimethylsulphonium salts, the decomposition must be a predominantly unimolecular process.

The decomposition of ethyldimethylsulphonium bromide provides an additional test. It is well established that the ease of ionisation is Et > Me, while in a bimolecular nucleophilic displacement the order is reversed. Ethyldimethylsulphonium bromide was decomposed at 100° in water and 4 : 1 water–dioxan. The mixture of sulphides obtained was analysed by gas chromatography. The $[Me_2S] : [EtSMe]$ ratio was determined by gas chromatography.

In water and in 4 : 1 water–dioxan the relative amount of dimethyl sulphide produced was 40 moles %, while that of ethyl methyl sulphide was 60 moles %. The concentration of methyl groups being double that of ethyl in this sulphonium salt, the ratio $\frac{1}{2}[EtSMe] : [Me_2S]$ can, to a first approximation,* be identified with the rate of substitution at a methyl group relative to that at an ethyl group, k_{Me}/k_{Et}. In the Table these rates are summarised, together with those obtained by Dostrovsky, Hughes, and Ingold [3] for alkyl bromides under predominantly unimolecular conditions.

Table

Solvent and temp.	Compound	k_{Me}/k_{Et}
H_2O–$H{\cdot}CO_2H$, 95°	RBr	0·64
Ag^+, 30% H_2O–70% EtOH, 64°	RBr	0·81
H_2O, 100°	$Et\overset{+}{S}Me_2\bar{B}r$	~0·75
80% H_2O–20% Dioxan, 100°	$Et\overset{+}{S}Me_2\bar{B}r$	~0·75

Under predominantly bimolecular conditions, *i.e.*, when ethyldimethylsulphonium bromide was decomposed in 4 : 1 water–dioxan at 100° in the presence of an equivalent amount of triethylamine, 11 moles % of dimethyl sulphide and 88 moles % of ethyl methyl sulphide were produced, leading to $\frac{1}{2}[EtSMe] : [Me_2S] = 4{\cdot}0$.

This result agrees with the expected relation for bimolecular nucleophilic substitutions, namely, $k_{Me} > k_{Et}$. The numerical value, however, provides only a lower minimum for the ratio (k_{Me}/k_{Et}) (S_N2) since under the experimental conditions some of the dimethyl sulphide is produced by a bimolecular elimination process ($E2$).

* This approximation neglects any possible small difference in the stability of EtSMe and SMe_2.

[1] Gleave, Hughes, and Ingold, *J.*, 1935, 236.
[2] Streitwieser, *Chem. Rev.*, 1956, **56**, 571.
[3] Dostrovsky, Hughes, and Ingold, *J.*, 1946, 190.

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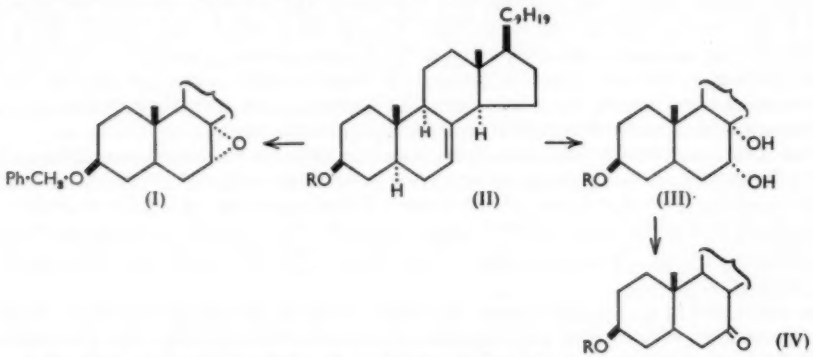
95. *Preparation of 3β-Hydroxyergostan-7-one.*

By G. D. MEAKINS and J. S. STEPHENSON.

IN work concerned with the properties of 9α-methyl-steroids [1] a method was required for converting Δ^7-stenols into the corresponding 7-ketones. This Note describes related experiments with ergost-7-enol.

The first approach involved conversion of ergost-7-enol (II; R = H) into the benzyl ether (II; R = CH_2Ph) which, with perbenzoic acid in benzene, gave the 7 : 8-epoxide (I) in excellent yield. Attempts to open the oxide ring by lithium aluminium hydride had no effect, even after prolonged refluxing in tetrahydrofuran.



Oxidation of the ether and ergost-7-enyl acetate (II; R = Ac) with osmium tetroxide yielded the 7α : 8α-diol (III; R = CH_2Ph) and the 3β : 7α : 8α-triol (III; R = H) respectively. [α-Configurations for the epoxide ring in (I) and the new hydroxyl groups in (III) are assumed on the general tendency for rear approach of peracids and osmium tetroxide to the steroid molecule; a close analogy is found in the oxidation of cholest-7-enyl acetate to cholestane-3β : 7α : 8α-triol.[2]] On treatment with methanolic sulphuric acid, the triol (III; R = H) was converted quantitatively into 3β-hydroxyergostan-7-one [3] (IV; R = H), further identified as the acetate [4] (IV; R = Ac). The reaction presumably proceeds by *trans*-elimination of the tertiary 8α-hydroxyl group and subsequent ketonisation. This route to 7-ketones is superior to the alternative (pyrolytic) method from 7 : 8-diols,[5] and to that involving isomerisation of 7 : 8-epoxides.[4]

Experimental.—General features were the same as those described elsewhere.[1]

3β-Benzyloxyergost-7-ene. A solution of ergost-7-en-3β-ol (400 mg.) and benzyl chloride (2 c.c.) in dioxan (10 c.c.) was heated at 100° with powdered potassium hydroxide (4 g.) for 1 hr. The residue obtained on filtration and evaporation *in vacuo* was extracted with light petroleum. The solution so obtained was washed with water and filtered through anhydrous sodium sulphate on to alumina (50 g.; Grade O). Elution with light petroleum–benzene (4 : 1; 150 c.c.) afforded the *benzyl ether* (400 mg.), m. p. 107—108·5° after crystallisation from methanol, $[\alpha]_D$ −1° (*c* 1·6) (Found: C, 85·9; H, 10·8. $C_{35}H_{54}O$ requires C, 85·65; H, 11·1%).

3β-Benzyloxy-7α : 8α-epoxyergostane. 3α-Benzyloxyergost-7-ene (2 g.) in benzene was

[1] Jones, Meakins, and Stephenson, unpublished work.
[2] Fieser and Ourisson, *J. Amer. Chem. Soc.*, 1953, **75**, 4404.
[3] Stavely and Bollenback, *ibid.*, 1943, **65**, 1290.
[4] Alt and Barton, *J.*, 1954, 1356.
[5] Pearlman and Wintersteiner, *J. Biol. Chem.*, 1939, **130**, 35.

treated with an excess of perbenzoic acid in benzene solution at −15° for 15 hr., and the mixture was then poured into dilute aqueous sodium hydrogen carbonate. Isolation with ether afforded the *oxide* (1·8 g.), m. p. 130—135°, which crystallised from ethyl acetate–ethanol to give the pure product, m. p. 136—138°, $[\alpha]_D$ −1° (*c* 1·05) (Found: C, 83·2; H, 10·8. $C_{35}H_{54}O_2$ requires C, 82·95; H, 10·7%). This compound was recovered unchanged after 6 hours' refluxing with lithium aluminium hydride in ether or tetrahydrofuran.

3β-*Benzyloxyergostane-7α : 8α-diol.* Osmium tetroxide (275 mg.) in ether (5·5 c.c.) was added to 3β-benzyloxyergost-7-ene (230 mg.) in a mixture of ether (2 c.c.) and pyridine (1 c.c.). The mixture was refluxed for 1 hr., then evaporated under reduced pressure. The residue was refluxed in tetrahydrofuran with an excess of lithium aluminium hydride for 30 min. After addition of ethyl acetate the mixture was stirred for 30 min. with water and extracted with ether. Standard manipulation gave the *diol* (150 mg.), m. p. 153—154·5° (from methanol). Recrystallisation afforded material with m. p. 155—157°, $[\alpha]_D$ −24° (*c* 1·0) (Found: C, 79·8; H, 10·5. $C_{35}H_{56}O_3$ requires C, 80·1; H, 10·8%).

Ergostane-3β : 7α : 8α-triol. (*a*) A mixture of osmium tetroxide (2 g.) in ether (25 c.c.) and 3β-acetoxyergost-7-ene (1·7 g.) in ether (25 c.c.)–pyridine (6 c.c.) was refluxed for 1 hr. After subsequent treatment with lithium aluminium hydride as in the preceding experiment, the mixture of products was adsorbed from benzene (20 c.c.) on deactivated alumina (140 g.). Benzene–ether (4 : 1; 250 c.c.) eluted ergost-7-en-3β-ol (400 mg.). A second fraction (1·15 g.), eluted with ether–methanol (50 : 1, 750 c.c.), crystallised from methanol to give the *triol*, m. p. 215—217° (dependent on rate of heating), $[\alpha]_D$ −16° (*c* 0·6) (Found: C, 77·4; H, 11·6. $C_{28}H_{50}O_3$ requires C, 77·4; H, 11·6%).

(*b*) 3β-Acetoxyergost-7-ene (0·8 g.) was converted into the osmic ester as described above. This ester was dissolved in a mixture of tetrahydrofuran (20 c.c.), dioxan (20 c.c.), and an aqueous solution (50 c.c.) containing potassium hydroxide (7·5 g.) and mannitol (7·5 g.). After 30 min. at 20° the mixture was diluted with water and extracted with ether. The material obtained by evaporation of the ether solution was treated with 10% ethanolic potassium hydroxide for 12 hr. at 20° to ensure complete hydrolysis of the 3-acetoxyl group. Dilution of the ethanolic solution with water and isolation with ether afforded the triol (0·6 g.), m. p. 216—218°, $[\alpha]_D$ −15° (*c* 1·0).

3β-*Hydroxyergostan-7-one.* A solution of the triol (400 mg.) in methanol (35 c.c.) was warmed with 10% methanolic sulphuric acid (35 c.c.) to 50°, then kept at 20° for 1·5 hr. Water was added and the product isolated by filtration. Crystallisation from methanol gave the *hydroxy-ketone* (342 mg.), m. p. 155—157° raised by recrystallisation to 156·5—157·5°, $[\alpha]_D$ −35° (*c* 1·15) (Found: C, 80·5; H, 11·6. $C_{28}H_{48}O_2$ requires C, 80·7; H, 11·6%), $\nu_{max.}$ 3606, 1709, and 1026 cm.$^{-1}$ (Stavely and Bollenback [3] report m. p. 154° but do not give analytical data).

Recovery of the compound unchanged after 2 hours' boiling with 10% ethanolic potassium hydroxide confirms its possession of the more stable (β)-configuration at position 8. Acetylation with acetic anhydride–pyridine at 20° gave 3β-acetoxyergostan-7-one, m. p. 188—190°, $[\alpha]_D$ −42° (cf. the values, m. p. 183—184°, $[\alpha]_D$ −42°,[3] and m. p. 178—180°, $[\alpha]_D$ −46° [4]). The 2 : 4-*dinitrophenylhydrazone*, crystallised from ethanol, had m. p. 257—258° (Found: C, 68·1; H, 8·6. $C_{34}H_{52}O_5N_4$ requires C, 68·4; H, 8·8%), $\lambda_{max.}$ 365 mμ (ε 23,000).

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96. *Substitution Compounds of Tristrifluoromethylphosphine with Nickel Carbonyl.*

By H. J. EMELÉUS and J. D. SMITH.

THE feeble donor properties of tristrifluoromethylphosphine have been noted [1] but little work has been done on the co-ordination of this compound to atoms which can donate electrons to the empty *d* orbitals of the phosphorus atom. The work of Reppe,[2] Wilkinson,[3]

[1] Bennett, Emeléus, and Haszeldine, *J.*, 1953, 1565.
[2] Reppe and Schweckendiek, *Annalen*, 1948, **560**, 104.
[3] Irvine and Wilkinson, *Science*, 1951, **113**, 742; Wilkinson, *J. Amer. Chem. Soc.*, 1951, **73**, 5501.

and Malatesta [4] showed that the carbonyl group in nickel carbonyl can be replaced by certain compounds of tervalent phosphorus, and suggested that tristrifluoromethylphosphine could form similar substitution compounds. Such compounds have now been prepared.

Nickel carbonyl and excess of tristrifluoromethylphosphine react in a sealed tube [5] or, better, in a system from which the carbon monoxide can escape, to form a mixture of $(CF_3)_3P{\cdot}Ni(CO)_3$ and $[(CF_3)_3P]_2Ni(CO)_2$. The reaction takes place at room temperature, but a higher temperature favours the formation of the disubstituted compound. This higher temperature must not be maintained for more than half an hour, as the products decompose slowly. Above 70° decomposition is rapid. The *products* can be separated by trap-to-trap distillation in the vacuum system, but completely pure materials have not been obtained. Hydrolysis at 100° by excess of sodium hydroxide solution yielded fluoroform, which was weighed in the vacuum system; nickel and phosphorus were estimated in the residual solution {Found: CF_3, 56·7; Ni, 14·3; P, 8·2%; *M*, 378; m. p. −71·5 to −70·5°. $(CF_3)_3P{\cdot}Ni(CO)_3$ requires CF_3, 54·4; Ni, 15·4; P, 8·1%; *M*, 381. Found: CF_3, 68·7; Ni, 9·5; m. p. −31·5 to −30°. $[(CF_3)_3P]_2Ni(CO)_2$ requires CF_3, 70·0; Ni, 9·9%}. The vapour pressure of $(CF_3)_3P{\cdot}Ni(CO)_3$ was measured by means of a mercury isoteniscope in the range 0—50° and obeyed the equation

$$\log p(\text{mm.}) = 7{\cdot}161 - 1629/T$$

Slight decomposition occurred. The extrapolated b. p. is 107·5° ± 1°, the latent heat 7450 cal./mole, and Trouton's constant, 19·6. The vapour pressure of $[(CF_3)_3P]_2Ni(CO)_2$ is less than 1 mm. at 20° and a vapour-pressure curve could not be obtained because of the thermal instability of the compound. The substitution compounds are colourless liquids, which remain quite clear when stored in sealed glass ampoules in the dark. They also seem stable to mercury. Exposure to bright sunlight causes them to turn red: the colour may be due to colloidal nickel. The compounds are spontaneously inflammable in air.

Tristrifluoromethylphosphine does not react with tetrakistrichlorophosphinenickel in a sealed tube at temperatures up to 60°, though at 80° complete decomposition of the mixture to nickel, tristrifluoromethylphosphine, and phosphorus trichloride occurs. It does not therefore seem possible to prepare tetrakistristrifluoromethylphosphinenickel $[(CF_3)_3P]_4Ni$ by methods analogous to those used by Wilkinson for the preparation of tetrakistrifluorophosphinenickel and tetrakistribromophosphinenickel. Tristrifluoromethylarsine and -stibine failed to yield substitution compounds.

One of us (J. D. S.) gratefully acknowledges a Maintenance Grant from the Department of Scientific and Industrial Research.

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[4] Malatesta and Sacco, *Ann. Chim.* (*Italy*), 1954, **44**, 134.
[5] Preliminary experiments were made by Dr. Ram Chand Paul here.

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97. *Studies on Phosphorylation. Part XVI.* Iodides as Debenzylating and Dealkylating Agents.*

By R. J. W. CREMLYN, G. W. KENNER, J. MATHER, and SIR ALEXANDER TODD.

ANIONIC debenzylation of phosphates, pyrophosphates, and phosphites is a conveniently selective technique of general application which has proved important in nucleotide synthesis. When it was first introduced, lithium chloride was the reagent used; [1] later, thiocyanates were found to react under milder conditions [2] but unfortunately they cannot be used if anionic debenzylation is to be followed directly by hydrogenation since the

* Part XV, *J.*, 1957, 1497.
[1] Clark and Todd, *J.*, 1950, 2030.
[2] Morrison and Atherton, B.P. 675,779.

product is usually contaminated by traces of thiocyanate. We have examined other reagents partly to overcome this difficulty and partly to make available a range of techniques needed for nucleotide synthesis. We considered primarily anions with high "nucleophilic constants."[3] Apart from those anions containing sulphur, iodide (5·04) and cyanide[4] (5·1) both stand above thiocyanate (4·77). Iodides proved very effective although, unfortunately, like the thiocyanates they could not be used as a preliminary to hydrogenolysis since iodide ion completely poisoned the usual palladised charcoal catalysts and largely inactivated Raney nickel. The practical value of iodides as reagents for both debenzylation and dealkylation makes it desirable to record our experiments. Since they were completed, experiments with sodium iodide and barium iodide have been described by Zervas and Dilaris;[5] with the exception of tribenzyl phosphate the esters studied by them were different so that the two investigations are complementary and cover most of the field.

Experiments with benzyl diphenyl phosphate showed that iodides react faster than thiocyanates and that the reaction is favoured by lowering the dielectric constant of the medium, as expected for a reaction of the S_N2 type.[6] Tribenzyl phosphate is much less reactive, as it is towards phenolic debenzylation.[7] Two preparations of practical value are those of monobenzyl phosphite and tribenzyl pyrophosphate through their sodium salts. They are slightly superior to the earlier methods, using ammonium thiocyanate[8] and 4-methylmorpholine[9] respectively.

Dealkylation, as well as debenzylation, can be accomplished with lithium chloride;[10] it is relatively rapid with calcium iodide, which usually gives nicely crystalline calcium salts. Variation of the alkyl group affects the velocity in the way typical of an S_N2 reaction, and naturally debenzylation is faster than dealkylations other than demethylation. Reactions between calcium iodide and benzyl dimethyl phosphate or dibenzyl methyl phosphate give mixtures of the debenzylated and demethylated phosphates.

A very convenient feature of all these preparations is the way in which the debenzylated or dealkylated salt separates, usually almost pure, from the reaction medium.

Experimental.—Debenzylation of benzyl diphenyl phosphate. A solution of benzyl diphenyl phosphate[7] (0·205 g.) and *cyclo*hexylammonium iodide, m. p. 197—199° (0·133 g., 1 mol.), in ethyl methyl ketone (5 c.c.) was boiled under reflux during 10 min. The precipitate of *cyclo*hexylammonium diphenyl phosphate,[10] m. p. 199—200° (0·182 g., 86%), was filtered off, washed, and dried. A parallel experiment with *cyclo*hexylammonium thiocyanate, m. p. 99—100°, gave 68% of the salt, while 98% was obtained with either reagent after 1 hour's boiling.

Heating at 51° during 20 min. gave the following yields of salts of diphenyl hydrogen phosphate from the various reagents: *cyclo*hexylammonium iodide, 44%; lithium iodide, 78%; sodium iodide, 62%; sodium thiocyanate, 10%. Runs with sodium iodide in methyl cyanide and 7 : 3 v/v ethyl methyl ketone–dioxan gave 32% and 65% respectively.

Reaction between sodium iodide and tribenzyl phosphate. Experiments like the preceding ones were made with both ethyl methyl ketone and methyl cyanide at 51°. There was no sign of sodium dibenzyl phosphate after 20 min. in either instance. With ethyl methyl ketone the yield was 25% after 1 hr., and with methyl cyanide 20% after 3 hr.

Debenzylation of dibenzyl phosphite. A solution of dibenzyl phosphite (5 g.) and sodium iodide (3·5 g., 1·2 mol.) in ethyl methyl ketone (40 c.c.) was boiled under reflux during 30 min. The precipitated *sodium benzyl phosphite* was recrystallised from aqueous acetone (3·2 g., 87%) (Found: C, 43·0; H, 3·9. $C_7H_8O_3PNa$ requires C, 43·3; H, 4·2%). A similar experiment with ammonium iodide, which dissolved gradually during 1 hr., gave 74% of ammonium benzyl phosphite.[8]

[3] Swain and Scott, *J. Amer. Chem. Soc.*, 1953, **75**, 141.
[4] Hawthorne, Hammond, and Graybill, *ibid.*, 1955, **77**, 486.
[5] Zervas and Dilaris, *ibid.*, 1955, **77**, 5354.
[6] Ingold, "Structure and Mechanism in Organic Chemistry," G. Bell, London, 1953, p. 347.
[7] Kenner and Mather, *J.*, 1956, 3524.
[8] Christie, Elmore, Kenner, Todd, and Weymouth, *J.*, 1953, 2947.
[9] Baddiley, Clark, Michalski, and Todd, *J.*, 1949, 815.
[10] Lecocq and Todd, *J.*, 1954, 2381.

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Debenzylation of tetrabenzyl pyrophosphate. (*a*) Removal of two benzyl groups. A solution of tetrabenzyl pyrophosphate (0·199 g.) and sodium iodide (0·110 g., 2 mol.) in ethyl methyl ketone (3 c.c.) was boiled under reflux during 40 min. There was very rapid deposition of *disodium* P^1P^2-*dibenzyl pyrophosphate* (0·125 g., 84%), which was recrystallised from aqueous acetone (Found: C, 41·7; H, 3·8. $C_{14}H_{14}O_7P_2Na_2$ requires C, 41·8; H, 3·5%). The same yield was obtained when the solution was boiled during 10 min. Paper chromatography [7] showed that no more than two benzyl groups can be removed in this way.

(*b*) Removal of one benzyl group. A solution of tetrabenzyl pyrophosphate (0·300 g.) and sodium iodide (0·083 g., 1 mol.) in methyl cyanide (15 c.c.) was kept at 51° for either 15 min., 30 min., or 1 hr. and then at 0° for 2 hr. The *sodium tribenzyl pyrophosphate* (53%, 58%, and 61%) was collected and recrystallised from aqueous ethyl methyl ketone (Found: C, 53·0; H, 4·7. $C_{21}H_{21}O_7P_2Na$ requires C, 53·2; H, 4·7%). A similar experiment with *cyclo*hexylammonium iodide (1 mol.) at four-fold concentration gave after 1 hr. at 51° and 15 hr. at 0° 65% of product, m. p. 115—118°. Recrystallisation from ethyl methyl ketone afforded cyclo*hexylammonium tribenzyl pyrophosphate*, m. p. 118—119° (Found: C, 59·3; H, 6·7. $C_{27}H_{35}O_7NP_2$ requires C, 59·2; H, 6·4%).

Dealkylation and debenzylation with calcium iodide. Commercial calcium iodide was dissolved in acetone, which was then diluted with chloroform and evaporated. After two repetitions of this drying process, the calcium iodide was recrystallised from acetone–ether and stored over phosphoric oxide as a colourless, very hygroscopic powder.

The necessary methyl esters were obtained from the corresponding acids and ethereal diazomethane in the usual way. *Methyl diphenyl phosphate* had n_D^{21} 1·5320 (Found: C, 58·9; H, 5·2. $C_{13}H_{13}O_4P$ requires C, 59·1; H, 4·9%). The other esters were made from dibenzyl or diphenyl phosphorochloridate by the procedure of Lecocq and Todd.[10]

A solution of the ester and calcium iodide (0·5 mol.) in ethyl methyl ketone was boiled under reflux during 3 hr. The precipitated calcium salt was washed thoroughly with acetone–ether, examined by ascending paper chromatography in butan-1-ol–water (86 : 14) on Whatman No. 1 paper, and recrystallised from aqueous ethanol or methanol–acetone.

The yields of calcium diphenyl phosphate from various alkyl diphenyl phosphates were 98% from methyl, 93% from *n*-propyl, 62% from *iso*propyl, 70% from *n*-butyl. Dimethyl phenyl phosphate furnished 87% of *calcium methyl phenyl phosphate*, m. p. above 300° (Found: C, 39·8; H, 3·9; P, 14·7. $C_{14}H_{16}O_8P_2Ca$ requires C, 40·4; H, 3·9; P, 14·9%).

One benzyl group was removed from the alkyl dibenzyl phosphates, giving the following products: *calcium benzyl ethyl phosphate*, m. p. 267—271°, R_F 0·52 (75%) (Found: C, 45·3; H, 5·2. $C_{16}H_{24}O_8P_2Ca$ requires C, 45·9; H, 5·1%); *calcium benzyl* n-*propyl phosphate*, m. p. 293—297°, R_F 0·58 (50%) (Found: C, 48·1; H, 5·4; P, 12·7. $C_{20}H_{28}O_8P_2Ca$ requires C, 48·2; H, 5·6; P, 12·5%); *calcium benzyl* iso*propyl phosphate*, m. p. 268—272°, R_F 0·58 (63%) (Found: C, 47·8; H, 5·9; P, 11·9%); *calcium benzyl* n-*butyl phosphate*, m. p. above 300°, R_F 0·68 (78%) (Found: C, 50·2; H, 6·0; P, 11·8. $C_{22}H_{32}O_8P_2Ca$ requires C, 50·2; H, 6·1; P, 11·8%); *calcium dibenzyl phosphate*, m. p. 261—263°, R_F 0·80 (87%) (Found: C, 55·9; H, 4·6; P, 9·9. $C_{28}H_{28}O_8P_2Ca$ requires C, 56·5; H, 4·7; P, 10·4%).

Subsequent experiments showed that the yield of precipitated calcium salt was generally between 60 and 70% after only 5 or 10 min. Experiments with boiling acetone solutions gave only 35—40% after 20 min., but the same yields as recorded above after 3 hr.

Dibenzyl methyl phosphate gave a calcium salt (Found: C, 48·9; H, 5·1; P, 11·7%) which appeared to be a mixture of calcium benzyl methyl phosphate, R_F 0·41, and calcium dibenzyl phosphate, R_F 0·80. Similarly benzyl dimethyl phosphate gave a calcium salt (Found: C, 31·1; H, 4·4; P, 16·2%) which was apparently a mixture of calcium benzyl methyl phosphate, R_F 0·40, and calcium dimethyl phosphate, R_F 0·56. In each case the yield of mixed calcium salts was about 75%.

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98. *The Oxidation of Some Naphthalene Derivatives with Peracetic Acid.*

By D. F. Downing and D. Woodcock.

Work on the metabolism of 2-methoxynaphthalene by *Aspergillus niger* van Tiegh required certain substituted 2-carboxycinnamic acids. Oxidation of naphthalene,[1] 1-naphthol,[2] and 2-naphthol [2,3,4] by peracetic acid has been previously used for the preparation of this acid, and this method using the appropriate substituted 2-naphthol was found to be the most convenient for the preparation of 2-carboxy-5-hydroxy-, -5-nitro-, and -3-nitro-cinnamic acid. The acids were easily isolated but yields were low (10—20%). 2-Carboxy-5-methoxycinnamic acid can also be prepared by this method but is obtained in better yield by methylation of the corresponding hydroxy-acid.

Experimental.—*2-Carboxy-5-hydroxycinnamic acid.* 2 : 6-Dihydroxynaphthalene [5] (1 g.) in acetic acid (5 ml.) was treated with 6—9% peracetic acid [6] (25 ml.) dropwise, during 0·5 hr., with stirring and kept at room temperature overnight. After removal of the solvent under reduced pressure, the residual brown solid was crystallised from water (charcoal), to give *2-carboxy-5-hydroxycinnamic acid* as colourless prisms (0·15 g.), m. p. 250—252° (decomp.) (after shrinkage) (Found: C, 57·8; H, 3·6. $C_{10}H_8O_5$ requires C, 57·7; H, 3·8%). In ethanol the acid gave a red-brown colour with a dilute solution of ferric chloride.

2-Carboxy-5-methoxycinnamic acid. (*a*) Methylation of the above acid (0·1 g.) with dimethyl sulphate in sodium hydroxide solution gave the *methoxy-acid* (0·09 g.) as prisms (from water), m. p. 186—187° (Found: C, 59·5; H, 4·5. $C_{11}H_{10}O_5$ requires C, 59·5; H, 4·5%). (*b*) 6-Methoxy-2-naphthol (see below) (0·3 g.) was oxidised with peracetic acid as described for 2 : 6-dihydroxynaphthalene (above). The acidic product (0·04 g.; m. p. 182—184°) gave no colour with dilute ferric chloride solution and did not depress the m. p. of the product from (*a*) above.

6-Methoxy-2 naphthol. 2 : 6-Dihydroxynaphthalene (3·2 g.) in methanol (20 ml.) was treated with dimethyl sulphate (2·5 ml.) and the mixture stirred at 30—40° during dropwise addition of sodium hydroxide (0·8 g.) in water (3 ml.). After a further 0·5 hour's stirring at the same temperature, water (20 ml.) was added and the solution extracted with ether. The naphtholic material isolated by extraction of the ethereal solution with 10% sodium hydroxide solution was a mixture of mono- and di-methyl ethers which were separated by fractional crystallisation from water, the latter ether being much less soluble. The *monomethyl ether*, recrystallised from water, formed colourless plates, m. p. 149—150° (Found: C, 75·7; H, 5·9. $C_{11}H_{10}O_2$ requires C, 75·9; H, 5·7%). Fischer and Hammerschmidt [7] and Windaus [8] give m. p. 136—137°.

2-Carboxy-5-nitrocinnamic acid. 6-Nitro-2-naphthol [9] (1 g.) in acetic acid (5 ml.) was treated as above with peracetic acid (16 g.). The solution remained at room temperature for two days, during which crystals were deposited. These were filtered off, washed with a little cold water, and recrystallised from 50% ethanol, to give pale yellow needles of *2-carboxy-5-nitrocinnamic acid*, m. p. 195—196° (Found: C, 50·7; H, 3·2; N, 6·1. $C_{10}H_7O_6N$ requires C, 50·6; H, 3·0; N, 5·9%).

2-Carboxy-3-nitrocinnamic acid. 8-Nitro-2-naphthol [10] (2·5 g.) was oxidised as described for 6-nitro-2-naphthol (above). Recrystallisation of the product gave pale yellow plates (from water), m. p. 188—189° (Found: C, 50·9; H, 2·7; N, 6·2%).

Department of Agriculture and Horticulture, University of Bristol, Research Station, Long Ashton, Bristol. [*Received, August 26th*, 1957.]

[1] Böeseken and Sloff, *Rec. Trav. chim.*, 1930, **49**, 100.
[2] Böeseken and von Konigsfeldt, *ibid.*, 1935, **54**, 313.
[3] Bigiavi and Cerchiai, *Atti R. Accad. Lincei*, 1922, **31**, II, 27.
[4] Greenspan, *Ind. Eng. Chem.*, 1947, **39**, 847.
[5] Willstätter and Parnas, *Ber.*, 1907, **40**, 1410.
[6] Swern, *Org. Reactions*, Vol. VII, p. 395.
[7] Fischer and Hammerschmidt, *J. prakt. Chem.*, 1916, **94**, 24.
[8] Windaus, *Ber.*, 1924, **57**, 1731.
[9] Hudson and Ward, *J.*, 1947, 327.
[10] Friedländer and Szymanski, *Ber.*, 1892, **25**, 2076.

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99. *The Reaction of Chlorosulphonic Acid with Aminophenols.*

By E. Boyland and D. Manson.

Wiley [1] prepared 2-amino-1-naphthyl hydrogen sulphate, which is a metabolite of 2-naphthylamine, by reaction of 2-amino-1-naphthol hydrochloride with chlorosulphonic (chlorosulphuric) acid in dimethylaniline and carbon disulphide. Boyland, Manson, and Sims [2] found that *o*-aminophenol and chlorosulphonic acid in pyridine yielded *o*-hydroxyphenylsulphamic acid. The formation of 7-hydroxy-2-naphthylsulphamic acid by reaction of chlorosulphonic acid with 2-amino-7-naphthol in quinoline has also been described.[3] These facts suggested that sulphuric esters or sulphamic acid derivatives of aminophenols might be obtained by varying the reaction medium. *o*-, *m*-, and *p*-Aminophenol and 2-amino-6-naphthol have been found to react with one equivalent of chlorosulphonic acid in pyridine and, in one case, in dimethylaniline, also, to give the sulphamic acid derivatives. In dimethylaniline and carbon disulphide the sulphuric esters were formed. In each case only a trace or none of the isomer was detected. Members of each pair of isomers were distinguished from each other by their R_F values and colour reactions. The sulphamic acid derivatives condensed only slowly with *p*-dimethylaminobenzaldehyde whereas the aminophenyl sulphuric esters reacted immediately. Both, however, diazotised immediately and coupled with hexylresorcinol. 2-Amino-6-naphthol hydrochloride gave both a sulphamic acid derivative and a sulphuric ester, but only the sulphuric acid ester was obtained from 2-amino-1-naphthol hydrochloride. Prolonging the reaction time of 2-amino-1-naphthol hydrochloride with chlorosulphonic acid diminished the yield of ester. Boyland, Manson, and Orr [4] found that the free base gave only the sulphuric ester of 1-hydroxy-2-naphthylsulphamic acid. *o*-Aminophenol gives both *o*-hydroxyphenylsulphamic acid and *o*-aminophenyl hydrogen sulphate, which is of interest in view of the existence of only *N*-acyl derivatives.

Experimental.—Paper chromatography was carried out on Whatman No. 1 chromatography paper, ascending development being used with propan-1-ol–butan-1-ol–0·1N-ammonia (1 : 2 : 1 v/v). The compounds were detected on chromatograms by the following reagents: (*a*) Ehrlich's reagent (*p*-dimethylaminobenzaldehyde, 0·5%, in ethanol containing 1 ml. of concentrated hydrochloric acid per 100 ml.); (*b*) N-hydrochloric acid followed by sodium nitrite (0·5%) and hexylresorcinol (0·5% in 2N-sodium hydroxide); (*c*) 10% aqueous sodium carbonate followed by diazotised sulphanilic acid [1·6 ml. sodium nitrite (0·5%) added to 10 ml. of sulphanilic acid (0·2% in N-hydrochloric acid)].

Sulphuric esters. o-Aminophenol (1·1 g.) was added with stirring to chlorosulphonic acid (1·1 g.), dimethylaniline (2 ml.), and carbon disulphide (10 ml.). After 16 hr. at room temperature, the mixture was poured into water containing potassium hydroxide (2 g.). The mixture was extracted several times with ether and then evaporated to dryness. The residue was extracted several times with hot methanol, and the combined extracts were evaporated to small bulk: *o*-aminophenyl potassium sulphate separated on cooling. After recrystallisation from aqueous ethanol 0·5 g. of ester was obtained (Found: S, 14·1. Calc. for $C_6H_6O_4NSK$: S, 14·1%). Under similar conditions *m*-aminophenol (5 g.) gave *m*-aminophenyl potassium sulphate (1·5 g.) (Found: N, 6·0; S, 14·0. Calc. for $C_6H_6O_4NSK$: N, 6·2; S, 14·1%), and similarly *p*-aminophenol (5 g.) gave *p*-aminophenyl potassium sulphate (1·3 g.) (Found: N, 5·9; S, 13·1. Calc. for $C_6H_6O_4NSK,H_2O$: N, 5·7; S, 13·1%). 2-Amino-6-naphthol hydrochloride (1·5 g.) in chlorosulphonic acid (0·9 g.), dimethylaniline (4·5 ml.), and carbon disulphide (27 ml.) gave 2-amino-6-naphthyl potassium sulphate (0·5 g.), needles (Found: N, 4·8; S, 11·6. Calc. for $C_{10}H_8O_4NSK$: N, 5·05; S, 11·55%). All the compounds gave precipitates when heated with 2N-hydrochloric acid and barium chloride. Paper chromatography of the mixtures showed that none or only a trace of the isomeric sulphamate was formed. The properties of

[1] Wiley, *J. Biol. Chem.*, 1938, **124**, 627.
[2] Boyland, Manson, and Sims, *J.*, 1953, 3623.
[3] F.P. 684,356.
[4] Boyland, Manson, and Orr, *Biochem. J.*, 1957, **65**, 417.

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the sulphuric esters on paper chromatograms are compared with those of the sulphamates in the Table. All the compounds gave yellow colours with Ehrlich's reagent. The colour reactions and analytical figures of the sulphuric esters agreed with those of the products obtained by the reduction of the corresponding nitro-derivatives.[5]

A: Diazotisation and coupling with hexylresorcinol.
B: Treatment with diazotised sulphanilic acid.

	R_F	A	B	R_F	A	B
	Aminophenyl hydrogen sulphate			Hydroxyphenylsulphamic acid		
o-Isomer	0·35	Orange	No colour	0·3	Mauve	Orange-red
m-Isomer	0·28	Orange-red	,,	0·22	Orange	Yellow
p-Isomer	0·21	Yellow	Yellow	0·2	Mauve	Pink
From	Hydrogen sulphate			Sulphamic acid		
6 : 2-NH_2·$C_{10}H_6$·OH	0·47	Orange	Pink	0·33	Red	Mauve
2 : 1-NH_2·$C_{10}H_6$·OH	0·58	Mauve	Pink	(0·16	Mauve	No colour) *

* Sulphate ester of sulphamic acid.

Sulphamates. The preparation of potassium *o*-hydroxyphenylsulphamate from chlorosulphonic acid and *o*-aminophenol in pyridine has been described.[2] *o*-Aminophenol (1·1 g.) in dimethylaniline (5 ml.) and chlorosulphonic acid (1·1 g.) also gave this sulphamic acid derivative (0·5 g.). *m*-Aminophenol (5 g.) was added to pyridine (25 ml.) containing chlorosulphonic acid (5·8 g.), and the solution kept at room temperature overnight. The solution was poured into water (100 ml.) containing potassium hydroxide (7·5 g.). The mixture was adjusted to pH 6·0 and extracted several times with ether, after which it was made alkaline and evaporated to dryness under reduced pressure. The residue was extracted with hot methanol, and the combined extracts were evaporated to dryness and crystallised from aqueous ethanol, to yield *potassium* m-*hydroxyphenylsulphamate* (2·5 g.; plates) (Found: N, 5·5; S, 13·0. $C_6H_6O_4NSK,H_2O$ requires N, 5·7; S, 13·1%). *p*-Aminophenol (5 g.) was treated in the same way, but the residue from the methanol extraction was tarry and required treatment on porous tile before crystallisation from aqueous ethanol, to yield *potassium* p-*hydroxyphenylsulphamate* (0·5 g.), needles (Found: N, 5·4; S, 12·2. $C_6H_4O_4NSK,2H_2O$ requires N, 5·3; S, 12·2%). The use of dimethylaniline gave much tar and no sulphamate. 2-Amino-6-naphthol hydrochloride (1 g.), in pyridine (5 ml.) containing chlorosulphonic acid (0·58 g.), was treated in the same way as the aminophenols and gave *potassium* 6-*hydroxy*-2-*naphthylsulphamate* (0·25 g.), plates (Found: N, 4·7; S, 10·8. $C_{10}H_8O_4NSK,H_2O$ requires N, 4·7; S, 10·9%). On evaporation of the ether extracts unchanged 2-amino-6-naphthol was recovered (0·25 g. as the hydrochloride). Potassium 6-hydroxy-2-naphthylsulphamate gave erratic analytical figures if it was dried at 100° and this and the other sulphamates were dried at room temperature. All the compounds gave precipitates with barium chloride in warm 2N-hydrochloric acid.

Reaction of 2-*amino*-1-*naphthol hydrochloride with chlorosulphonic acid.* This hydrochloride (6 g.) was added to dimethylaniline (20 ml.), chlorosulphonic acid (3·5 g.), and carbon disulphide (100 ml.). The mixture was kept for 16 hr. at room temperature and added to water (100 ml.) containing potassium hydroxide (5 g.). The whole was extracted several times with benzene, evaporated to small volume under reduced pressure, and cooled, to yield 2-amino-1-naphthyl potassium sulphate (2·3 g.), plates. The mother-liquors were then evaporated to dryness, the residue dissolved in the minimum amount of a mixture of butan-1-ol, propan-1-ol, and water (2 : 1 : 1 v/v) and sufficient Whatman cellulose powder added to form a paste. A cellulose column (12 × 3 cm.) was prepared with the same solvent mixture, the paste added to the top, and the column developed and eluted with the solvent mixture, collection of fractions being guided by paper chromatography. The fraction containing 2-amino-1-naphthyl sulphuric ester yielded 0·7 g. as the potassium salt. Continued elution of the column gave fractions containing a trace of the sulphuric ester of 1-hydroxy-2-naphthylsulphamic acid.[4] The total yield of 2-amino-1-naphthyl potassium sulphate (Found: N, 5·3%) was 35%, which is more than was obtained when the free acid was isolated.[3] The preparation was repeated, the reaction being allowed to proceed at room temperature for 3 days. The alkaline aqueous solution of the products was evaporated to dryness and the residue chromatographed on a cellulose column as before. Fractions containing 2-amino-1-naphthyl potassium sulphate (300 mg.) and the

[5] Burkhardt and Wood, *J.*, 1929, 141; Bernstein and McGilvery, *J. Biol. Chem.*, 1952, **198**, 195; Booth, Boyland, and Manson, *Biochem. J.*, 1955, **60**, 62.

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dipotassium salt of the sulphuric ester of 1-hydroxy-2-naphthylsulphamic acid (60 mg.) (Found: N, 3·3; S, 16·25. Calc. for $C_{10}H_7O_7NS_2K_2$: N, 3·5; S, 16·2%) were obtained. The properties of these compounds were the same as those of previous preparations.[3,4] 1-Hydroxy-2-naphthylsulphamic acid could not be prepared by reaction of the aminonaphthol with chlorosulphonic acid in pyridine or dimethylaniline.

Analyses were carried out by Mr. P. Baker of Wellcome Research Laboratories. The work has been supported by grants to this Institute from the British Empire Cancer Campaign, the Jane Coffin Childs Memorial Fund for Medical Research, the Anna Fuller Fund, and the National Cancer Institute of the National Institutes of Health, U.S. Public Health Service.

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100. *Vapour Pressure of* NN′-*Diphenylacetamidine.*

By A. S. DUNN and A. HANRAHAN.

THE vapour pressure of *NN′*-diphenylacetamidine has been determined by Knudsen's effusion method[1] over the range 70—110°. The rate of effusion of the vapour through an orifice, measured by means of the contraction of a spiral spring, was related to vapour pressure by calibrating the orifice with stable solid benzophenone, whose vapour pressure was accurately determined by Neumann and Völker[2] as $4 + \log p^b(\text{mm}) = 17{\cdot}46 - (4966/T)$ where p^b is the vapour pressure of benzophenone and T the absolute temperature. The vapour pressure p of the substance is calculated from the p^b at the same rate of effusion by means of the relation $p = p^b[(M_b/M)(T/T_b)]^{\frac{1}{2}}$, where M and T are the molecular weight and absolute temperature of the substance and M_b, T_b those of benzophenone.

The vapour pressures of *NN′*-diphenylacetamidine at various temperatures thus measured are as follows:

Orifice diam. (in.)	0·025				0·050				
Temp. (°c)	110·0	105·0	100·0	95·0	90·0	86·6	83·4	80·0	70·0
$10^3 \times$ Pressure (mm. Hg)	26·45	16·31	9·26	5·46	3·45	2·364	1·315	1·102	0·302

The points were fitted by the method of least squares which gave the relation

$$4 + \log p = 19{\cdot}156 \pm 0{\cdot}038 - (6409{\cdot}2 \pm 136{\cdot}8)/T$$

The limits quoted are the standard errors.

The latent heat of sublimation of diphenylacetamidine was derived as $29{\cdot}3 \pm 0{\cdot}9$ kcal./mole.

Experimental.—Majury's apparatus[3] was used. The "Pyrex" glass spring was similar to that used by him but had a sensitivity of 3·39 mg./mm. The orifices were those calibrated by Majury and a check point with benzophenone fell precisely on his calibration. Two orifices, diameters 0·025 and 0·05 in. were used. The points obtained were satisfactorily collinear apart from one with the larger orifice at 100° where the rate of effusion was 0·275 mg./min.; evidently this rate was too great for the required conditions to be satisfied. All other rates of effusion were less than 0·2 mg./min.

NN′-Diphenylacetamidine, received from British Celanese Ltd. and recrystallised from methylated spirit, had m. p. 131° (uncorr.). Before use it was sublimed *in vacuo* at about 96° on a finger cooled by solid carbon dioxide–methanol, with continuous pumping to free it from occluded solvent.

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WYTHENSHAWE, MANCHESTER, 22. [*Received, September 25*, 1957.]

[1] Knudsen, *Ann. Physik*, 1909, **28**, 999.
[2] Neumann and Völker, *Z. phys. Chem.*, 1932, **161**, *A*, 33.
[3] Majury, *J. Soc. Dyers Colourists*, 1956, **72**, 41.

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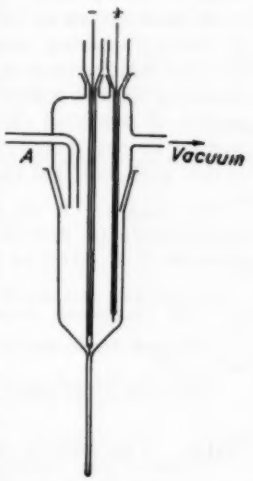
101. *Organomercury Groups. Part II.*[1] *Electron Resonance Measurements.*

By B. G. Gowenlock, P. Pritchard Jones, and D. W. Ovenall.

In a recent investigation and extension [1] of Kraus's work [2] on organomercury groups, it was suggested that they were best described in terms of " organic metals " or the Pauling theory of metals. It was also shown chemically that free-radical behaviour participated to only a very minor extent. To obtain further evidence for the understanding of these novel substances, the methyl-, *iso*propyl-, and *n*-butyl-mercury groups, prepared as cathode deposits on electrolysis of organomercuric chlorides in liquid ammonia, were examined at 90° K in an electron resonance spectrometer. No resonance absorption being detected, we infer that the organomercury groups do not contain free radicals.

Experimental.—A modification of Gowenlock and Trotman's method for the electrolytic production of organomercury groups was employed. Liquid ammonia was saturated with RHgCl (R = Me, Pr^i, Bu^n) and then carefully displaced into the glass reaction vessel shown, at *A*: these operations and the electrolysis were carried out at −78°. The cathode was mounted just above the narrow tube (external diam. 5 mm.) attached to the reaction vessel. In the case of the methyl group gentle tapping of the vessel sufficed to detach the small particles of the solid from the cathode and to send them to the bottom of the tube. For the *iso*propyl and *n*-butyl groups it was necessary to remove the bath of solid carbon dioxide and warm the tube carefully by hand. The subsequent violent agitation of the liquid ammonia removed the group from the cathode and the heavy solid settled when the cooling bath was replaced. A run of about 3 hr. was sufficient to give a layer of 1 in. depth in the narrow tube. Air was then admitted, the vessel and contents were detached, and most of the liquid ammonia was sucked off under vacuum. The vessel then contained the solid group at the base of the narrow tube covered by some six inches of liquid ammonia. The whole was then immersed in liquid oxygen, air admitted, the reaction vessel detached, and the narrow portion of the tube studied at 90° K in the electron resonance spectrometer of Abraham, Ovenall, and Whiffen.[3] It is very unlikely that oxygen from the air can diffuse through the liquid ammonia (15 in. depth) or through the solid ammonia (at least 6 in. depth) and react with the solid at the base of the narrow tube. At 90° K there is no detectable decomposition of the groups and the solid ammonia present has little or no dielectric loss at the microwave frequency. Absorptions were sought at a microwave frequency of approximately 9300 Mc./sec. over the magnetic-field range 1·9—3·5 kilogauss, which corresponds to the range of " *g* " values 4·55 to 1·9, but none was detected.



Discussion.—It is difficult accurately to estimate the detection limit of the spectrometer since this is directly proportional to the line width of the resonance. However, if it is assumed that the microwave cavity contained about 200 mg. of each group and that the resonance expected had a half-height width of 50 gauss, the sensitivity was such that one unpaired electron per 10^4 RHg units would have been detected. A theoretical study of the CH_3Hg radical [4] has shown that the wave function of the unpaired electron is represented predominantly by the term involving a free methyl radical at the van der Waals distance from a mercury atom in the ground state. This implies that the angular

[1] The paper by Gowenlock and Trotman, *J.*, 1957, 2114, is regarded as Part I.
[2] Kraus, *J. Amer. Chem. Soc.*, 1913, **35**, 1732.
[3] Abraham, Ovenall, and Whiffen, to be published.
[4] Gowenlock, Polanyi, and Warhurst, *Proc. Roy. Soc.*, 1953, *A*, **219**, 270.

momentum of the unpaired electron would be quenched, and that the resonance would occur not far from $g = 2{\cdot}00$. In view of the fact that over a wide range of g values, as well as near $g = 2{\cdot}00$, no resonance was detected, the RHg radical structure can be discounted. This is in accord with the lack of radical reactivity already demonstrated.[1]

From previous evidence it was concluded [1] that the groups were best described in terms of organic metals, and that the plausible assumption of an organomercurous compound was untenable. The data here presented afford no evidence against organomercurous compounds. Rochow, Hurd, and Lewis [5] recently stated that the groups are not mercurous compounds but gave no evidence for this assumption. It may be expected, if the metal theory for the groups be correct, that resonance from conduction electrons would be observed. However such resonance absorption has been detected only when a metal was in the form of particles small compared with the microwave skin depth. Thus Solt and Strandberg's [6] measurements on particles of sodium less than 4μ in diameter gave a g value of $2{\cdot}0014 \pm 0{\cdot}0002$ and a line-width of 10 gauss. Therefore, it seems unlikely because of particle size that conduction electrons would have been detected in the present investigation. Another possible objection to the metal theory of the groups would be that if they behaved as metals the microwave field patterns inside the cavity would be distorted and tuning would be difficult. No such difficulties were experienced, the groups behaving similarly to normal non-metallic samples. With samples of both zinc dust and mercury at 90° K it was impossible to tune and consequently pure metallic behaviour for the groups is difficult to uphold. However it was possible to tune when samples of powdered chalk containing up to 15 molar % of zinc dust were placed in the cavity. It may therefore be concluded that partial metallic behaviour is not disproved by this work, but that the groups cannot be regarded as radicals or pure metals.

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Department of Chemistry,
The University, Birmingham, 15. [*Received, September 30th*, 1957.]

[5] Rochow, Hurd, and Lewis, "The Chemistry of Organometallic Compounds," Wiley, New York, 1957, p. 121.
[6] Solt and Strandberg, *Phys. Rev.*, 1954, **95**, 607.

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102. *The Dipole Moment of* 5 : 5′-spiro*Bis*-1 : 3-*dioxan: A Correction.*

By I. T. Millar, C. T. Mortimer, and H. D. Springall.

Professor R. J. W. Le Fèvre has kindly drawn our attention to the marked difference between the value for the dipole moment of 5 : 5′-*spiro*bis-1 : 3-dioxan recorded in his recent paper [1] ($\mu = 2{\cdot}69$ D in carbon tetrachloride) and that recorded recently by us [2] ($\mu = 0$ D in benzene). We have recalculated the moment from our experimental data by the established expressions for ${}_{T}P_{2}$ and ${}_{E}P_{2}$ and have found an arithmetical error in the earlier record.

Our experimental data, in fact, yield for this compound values of ${}_{T}P_{2}$, ${}_{E}P_{2}$, and μ of 179·3 c.c., 34·3 c.c., and 2·66 D, respectively, in close agreement with the corresponding values found by Professor Le Fèvre and his collaborators.

This error invalidates the final piece of supporting evidence we adduced [2] but does not affect the general argument as to the freedom of rotation about the CH_2–O bonds in pentaerythritol and its derivatives.

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Keele, Staffordshire. [*Received, November 14th*, 1957.]

[1] Le Fèvre, Le Fèvre, and Smith, *J.*, 1958, **16**.
[2] Millar, Mortimer, and Springall, *J.*, 1957, 3456.